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11 CENTERS FOR MEDICARE AND MEDICAID SERVICES

12 Medicare Coverage Advisory Committee

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19 May 24, 2005

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21 Centers for Medicare and Medicaid Services

22 7500 Security Boulevard

23 Baltimore, Maryland

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1 Panelists  
2  
3 Vice Chairperson  
4 Barbara J. McNeil, M.D., Ph.D.  
5  
6 Voting Members  
7 Harry B. Burke, M.D., Ph.D.  
8 Mark Fendrick, M.D.  
9 Alexander H. Krist, M.D.  
10 Stephen L. Ondra, M.D.  
11 Mary Starmann-Harrison, B.S.N., M.H.S.A.  
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18 Charles J. Queenan, III  
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1 Panelists (Continued)  
2  
3 Guest Expert Panelists  
4 James Weinstein, M.D.  
5 Sean D. Sullivan, Ph.D.  
6 Richard G. Fessler, M.D., Ph.D.  
7 Daniel K. Resnick, Ph.D.  
8 David F. Kallmes. M.D.  
9 Jeffrey G. Jarvik, M.D., M.P.H.  
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11 Executive Secretary  
12 Kimberly Long  
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1 PANEL PROCEEDINGS

2 (The meeting was called to order at  
3 8:06 a.m., Tuesday, May 24, 2005.)

4 MS. LONG: Good morning and welcome,  
5 committee chairperson, members and guests. The  
6 committee is here today to discuss the evidence,  
7 hear presentations and public comments, and make  
8 recommendations regarding the treatment of  
9 vertebral body compression fractures.  
10 The following announcement addresses  
11 conflict of interest issues associated with this  
12 meeting and is made part of the record. The  
13 conflict of interest statute prohibits special  
14 government employees from participating in matters  
15 that could affect their or their employer's  
16 financial interests. To determine if any conflict  
17 existed, the Agency reviewed all financial  
18 interests reported by the committee participants.  
19 The Agency has determined that all members may  
20 participate in the matters before the committee  
21 today. With respect to all other participants, we  
22 ask in the interests of fairness that all persons  
23 making statements or presentations disclose any  
24 current or previous financial involvement in any  
25 orthopedic device company. This includes direct

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1 financial investment, consulting fees and  
2 significant institutional support. If you haven't  
3 already received a disclosure statement, they are  
4 available on the table outside of this room.  
5 We ask that all presenters please  
6 adhere to their time limit. We have a large  
7 number of presenters to hear from today and a very  
8 tight agenda, and therefore cannot allow extra  
9 time. There is a timer at the podium that you  
10 should follow. The light will begin flashing when  
11 there are two minutes remaining, and then turn red  
12 when your time is up. Please note that there is a  
13 chair in front of the stage for the next speaker.  
14 Please proceed to the chair when it is your turn.  
15 For the record, voting members present  
16 for today's meeting are Harry Burke, Mark  
17 Fendrick, Alex Krist, Stephen Ondra, Mary  
18 Starmann-Harrison, and Jonathan Weiner. A quorum  
19 is present and no one has been recused because of  
20 conflicts of interest. The entire panel,  
21 including non-voting members, will participate in  
22 the voting. The voting scores will be displayed  
23 on the screen following the meeting. Two averages  
24 will be calculated, one for the voting members and  
25 one for the entire panel.



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1 And one more brief announcement. If  
2 anyone is requiring transportation following the  
3 meeting, you should sign up at the registration  
4 desk during the break.  
5 I would like to now turn the meeting  
6 over to Dr. Steve Phurrough.  
7 DR. PHURROUGH: Good morning. I am  
8 Steve Phurrough, the director of the coverage and  
9 analysis group here at CMS and the CMS liaison for  
10 this particular meeting. Let me welcome you. A  
11 particular welcome to the panel and our  
12 appreciation for their taking time from their busy  
13 schedules to assist us in these deliberations.  
14 This is one, the beginning of a series  
15 of public meetings we expect to have over the next  
16 two to three years about issues surrounding spinal  
17 surgery. Spinal surgery is very common in our  
18 patient population in that they have lots of  
19 spinal disease, and we're interested in discussing  
20 what the evidence base is for those various  
21 procedures, and then perhaps providing guidance to  
22 the public on the other kinds of evidence that may  
23 be necessary to fully answer some of the questions  
24 regarding what is appropriate. We do not  
25 currently have a national coverage determination

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1 on spinal surgery, though we may in the future,  
2 depending on some of the evidence reviews that we  
3 do. So we look forward to a good discussion,  
4 thank you again for your participation and  
5 willingness to assist us in what we think are  
6 important topics for CMS. Barbara.  
7 DR. MCNEIL: Thank you again. I think  
8 this will be a very interesting day. We have had  
9 lots of material to review over the past week or  
10 so and will look forward to hearing additional  
11 presentations from the public and the various  
12 individuals who have signed up in advance. And I  
13 would just echo Kim's comments that we have a  
14 really tight schedule so your adherence to the  
15 time limits will be very much appreciated. And I  
16 would also like to ask you if you can, to be sure  
17 that you tell us as much as you think we're going  
18 to need during your presentations when it comes to  
19 our review of the voting questions. After lunch,  
20 the committee will be largely deliberating on its  
21 own. While we may ask a question or two of the  
22 audience, we expect to get most of the information  
23 from you from your morning session, from your  
24 morning presentations. So try to anticipate our  
25 needs.

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1 So with that, I would like to ask  
2 Dr. Feinglass to present the voting questions.  
3 Actually, while we're setting up, why don't we  
4 have the panel introduce themselves and whether or  
5 not they have any conflict of interest that they  
6 would like to discuss. So, we can start with Dr.  
7 Weinstein.  
8 DR. WEINSTEIN: Jim Weinstein from  
9 Dartmouth. I'm currently editor in chief of  
10 Spine. I also serve on various organizational  
11 boards for the American Academy of Orthopedic  
12 Surgery, the American Board of Orthopedic Surgery.  
13 I have recently been put on the board for United  
14 Health Care. I have funding from NIH, some CMS  
15 funding, and I'm trying to think of the third one,  
16 but I don't believe I have any conflicts related  
17 to this discussion.  
18 DR. JARVIK: I'm Jerry Jarvik from the  
19 University of Washington, I am chief of  
20 neuroradiology there. I do not have any conflicts  
21 of interest.  
22 DR. KALLMES: I am David Kallmes, from  
23 the Mayo Clinic. I do receive funding from NIH  
24 and don't have any conflicts.  
25 DR. RESNICK: I am Dan Resnick, from

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1 the University of Wisconsin in their spine  
2 section, am ex-chairman of Guidelines. I do have  
3 a consulting arrangement with Medtronic that has  
4 been disclosed previously.  
5 DR. R.G. FESSLER: Richard Fessler, I'm  
6 chief of neurosurgery at the University of  
7 Chicago. I developed a vertebroplasty set which  
8 is not marketed in the United States so I don't  
9 think it's a conflict of interest.  
10 DR. SULLIVAN: I'm John Sullivan, from  
11 the University of Washington, where I direct the  
12 technology assessment program. I have no  
13 conflicts.  
14 MR. QUEENAN: I'm Charlie Queenan, the  
15 consumer representative. I am an independent  
16 consultant and have no conflicts.  
17 MS. STARMANN-HARRISON: Mary  
18 Starmann-Harrison, with SSM Health Care, and I  
19 have no conflicts.  
20 DR. ONDRA: Steve Ondra, Northwestern  
21 University, and I have no conflicts pertinent to  
22 this. I have consulting arrangements with  
23 Medtronic and DePuy Spine.  
24 DR. KRIST: I'm Alex Krist, with the  
25 department of family medicine at Virginia

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1 Commonwealth University, and I have no conflicts  
2 of interest.  
3 DR. FENDRICK: Mark Fendrick,  
4 University of Michigan, no conflicts.  
5 DR. BURKE: Harry Burke, George  
6 Washington University, no conflicts.  
7 DR. MCNEIL: Barbara McNeil, Harvard  
8 Medical School and Brigham and Women's Hospital,  
9 no conflicts.  
10 Okay. Why don't we proceed with the  
11 questions.  
12 DR. FEINGLASS: Good morning. Thanks  
13 for coming to Baltimore on a slightly rainy day.  
14 As Steve mentioned, we are looking at several  
15 different things at CMS related to the spine. As  
16 you know, back pain is a significant concern for  
17 our beneficiaries. There are some important and  
18 long-term examinations that need to be done with  
19 the spine from our perspective. There is a  
20 substantial public health impact, leading to a lot  
21 of discomfort, loss of mobility, and serious  
22 morbidity.  
23 The back diseases of interest to us at  
24 this time are degenerative disk disease,  
25 degenerative spine disease, and vertebral

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1 compression fractures, which we are addressing  
2 today. As a quick overview, and you will hear  
3 more of this throughout the day, but  
4 vertebroplasty and kyphoplasty are both minimally  
5 invasive treatments. They insert bone cement into  
6 the compressed and fractured vertebrae to provide  
7 mechanical stabilization.  
8 Kyphoplasty is a variation of  
9 vertebroplasty. It uses an inflatable balloon to  
10 expand the compressed vertebral body, it attempts  
11 to restore natural vertebral height before  
12 injecting the cement-like substance, and attempts  
13 to correct spinal deformity.  
14 This is the review of the questions for  
15 today. They're divided into questions addressing  
16 vertebroplasty and questions addressing  
17 kyphoplasty.  
18 Number one: How well does the evidence  
19 address the effectiveness of vertebroplasty for  
20 patients with compression fracture as compared to  
21 conservative care?  
22 How confident are you in the validity  
23 of the scientific data on the following outcomes:  
24 Short-term morbidity, long-term morbidity,  
25 mortality, mobility-functional status, pain

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1 relief, with respect to vertebroplasty for  
2 patients with acute and subacute compression  
3 fracture or chronic compression fracture?  
4 How likely is it that vertebroplasty,  
5 in the following circumstances, acute and subacute  
6 compression fracture and chronic compression  
7 fracture, will positively affect the following  
8 outcomes: Short-term morbidity, long-term  
9 morbidity, mortality, mobility-functional status,  
10 and pain relief, when compared to conservative  
11 care?  
12 How confident are you that  
13 vertebroplasty will produce a clinically important  
14 net health benefit for patients with a compression  
15 fracture as compared to conservative care for  
16 patients with acute or subacute compression  
17 fracture or chronic compression fracture?  
18 Based on the literature presented, how  
19 likely is it that the results of vertebroplasty in  
20 the treatment of relief of pain and improvement in  
21 ability to function for patients with a  
22 compression fracture can be generalized to the  
23 Medicare population, or providers in community  
24 practice?  
25 These are the questions addressing

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1 kyphoplasty. How well does the evidence address  
2 the effectiveness of kyphoplasty for patients with  
3 compression fracture as compared to conservative  
4 care?  
5 How confident are you in the validity  
6 of the scientific data on the following outcomes:  
7 Short-term morbidity, long-term morbidity,  
8 mortality, mobility-functional status, pain  
9 relief, with respect to kyphoplasty for patients  
10 with acute and subacute compression fracture or  
11 chronic compression fracture?  
12 How likely is it that kyphoplasty, in  
13 acute and subacute compression fracture or chronic  
14 compression fracture, will positively affect the  
15 following outcomes when compared to conservative  
16 care: Short-term morbidity, long-term morbidity,  
17 mortality, mobility-functional status, pain  
18 relief?  
19 How confident are you that kyphoplasty  
20 will produce a clinically important net health  
21 benefit for patients with a compression fracture  
22 as compared to conservative care for patients with  
23 acute/subacute compression fracture or chronic  
24 compression fracture?  
25 And the final question. Based on the



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1 literature presented, how likely is it that the  
2 results of kyphoplasty in the treatment of relief  
3 of pain and improvement in ability to function for  
4 patients with a compression fracture can be  
5 generalized to the Medicare population or  
6 providers in community practice?  
7 Thank you.  
8 DR. MCNEIL: Thank you, Dr. Feinglass.  
9 Dr. Mark.  
10 DR. MARK: Thank you for inviting me.  
11 I see in the schedule that what I'm doing is  
12 presenting the results of our TA, and I'll explain  
13 what that TA is. TA stands for technology  
14 assessment, and at the Blue Cross Blue Shield  
15 Association we periodically review procedures,  
16 diagnostic tests, surgical procedures, and we try  
17 to do an objective review of the literature and  
18 apply certain criteria to the selection of studies  
19 for quality, and evaluate and synthesize the data  
20 from these studies and see if they meet our  
21 criteria. Our reports for Blue Cross Blue Shield  
22 Association are reviewed by an independent panel  
23 and then these reports are forwarded to the Blue  
24 Cross plans for them to make a coverage decision.  
25 So in our review, we try to set a

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1 minimum quality standard for selecting articles  
2 and then we try to establish a format for  
3 extracting all the data from those studies so that  
4 it's in a way that could be easily visualized,  
5 look at subgroup outcomes if possible or  
6 necessary, and then for Blue Cross Blue Shield  
7 Association, we have a specific set of criteria  
8 that we apply to see if the procedure is effective  
9 or not.  
10 For this particular, for the topics of  
11 vertebroplasty and kyphoplasty, we used these  
12 selection procedures for studies. We looked for  
13 full-length English language studies, although  
14 there will be a few exceptions that I will mention  
15 below. We wanted to select studies that had a  
16 clinical indication for osteoporosis or  
17 malignancy, and that they fully reported a  
18 consecutive or near consecutive series of  
19 patients, the studies identified a current  
20 procedure, and that they studied relevant outcomes  
21 of pain, functional status or quality of life. We  
22 did not select studies that had purely anatomic  
23 outcomes, and we will see that in several of the  
24 studies some researchers report changes in the  
25 anatomic shape of the spine, but we did not look

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1 at that directly as an outcome.  
2 As a slice to attempt to get better  
3 quality studies, we wanted studies that looked at  
4 both pre and post-procedure assessments of these  
5 outcomes. Some studies will only report  
6 retrospectively after the procedure, asking the  
7 patient, how do you feel after the procedure, and  
8 we felt this was not as rigorous a method for  
9 assessing outcomes.  
10 And just to cull the literature for a  
11 reasonable quantity of studies, we set a minimal  
12 sample size of 20 patients for osteoporosis, and  
13 because they were used less frequently for  
14 patients with malignant processes in their back, a  
15 slightly smaller sample size. And this wasn't a  
16 rigorously determined, statistically driven sample  
17 size, it was meant to be practical and to be  
18 overly generous in including studies. If we were  
19 looking for something more statistically rigorous,  
20 we would have upped the sample size, but this  
21 leaves a sufficient number to examine.  
22 In our exceptions for published  
23 literature, we had several reviewers and they  
24 directed us to comparative trials, either  
25 randomized clinical trials or nonrandomized

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1 comparative studies, and where these were  
2 available, we accepted what information was  
3 available in abstract form or from foreign  
4 literature. So, we were particularly interested  
5 in trying to find those studies which actually  
6 compared vertebroplasty or kyphoplasty to other  
7 procedures.  
8 And what we didn't include would be a  
9 lot of the biomechanics, biomechanical type  
10 studies. Vertebroplasty and kyphoplasty are used  
11 for other diseases, angioma of the spine is a  
12 common indication and that was not in our review  
13 this time.  
14 Non-health-related outcomes, we did not  
15 look at case reports, although our full technology  
16 assessment does have a review of complications  
17 that are known about and discussed.  
18 And there are some other important  
19 questions that are sometimes in the review of our  
20 technology assessments, but given our time and  
21 space, we didn't cover those as comprehensively.  
22 For example, for these procedures, an important  
23 question that the evidence is probably not in on,  
24 is there a risk of future fracture after you have  
25 had the procedure, does vertebroplasty make it

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1 more likely to have a subsequent fracture  
2 elsewhere, and that's a complicated question. My  
3 feeling is that the literature is probably  
4 incomplete on that question, but we did not  
5 address that in a fully comprehensive way in this  
6 review.  
7 Now, one of the challenges in trying to  
8 view this literature is that there is a variety,  
9 even though we had a criteria for outcome  
10 measures, there is many ways to measure outcomes,  
11 and even within one method, there are many  
12 variations, and it's probably a course or a day's  
13 lecture to try to study each of the properties of  
14 the measurement scales. So, I can't do that so  
15 let me just summarize what we have.  
16 There are various methods of measuring  
17 pain on a visual analog scale, and a visual analog  
18 scale is just like a picture of a thermometer, and  
19 the patient rates how bad their pain is. So it's  
20 usually classically on a one to ten scale, but in  
21 many of these studies, the visual analog scale was  
22 a series of questions, so not just one question,  
23 but a series of questions asking about back pain,  
24 at rest, doing various activities, daily living  
25 things, so the visual analog scale is many

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1 different things, not just one thing in these  
2 studies.  
3 There are studies of function and there  
4 are studies of function specific to back pain, and  
5 probably the best known one is the Oswestry  
6 Disability Index, which is a series of ten  
7 questions and five choices for each question, and  
8 it's most commonly expressed as a zero to 100  
9 scale. People with bad back pain tend to be  
10 between 50 and 60 and classically, people have  
11 thought that a difference of five to 15 is a  
12 clinically significant change in this score.  
13 According to some documents in the FDA in terms of  
14 evaluating procedures, they like to see a 15-point  
15 difference in that scale as a clinically important  
16 change.  
17 Again these scales, even if they were  
18 developed for back pain, may not have been  
19 investigated in depth for this particular subgroup  
20 of patients, so that a scale for that particular  
21 measurement may be insensitive to the degree of  
22 pain. So scales have ceiling effects where you  
23 hurt so bad that the scale doesn't differentiate  
24 that, or where you have floor effects where people  
25 are trying to differentiate a level of pain that

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1 the scale's insensitive to. So it's a very  
2 difficult art to kind of tease out what's going on  
3 from what we pick up from the patients concerning  
4 pain.  
5 There is some quality of life types of  
6 outcomes that some of these studies use. One  
7 study uses a questionnaire specific to  
8 osteoporosis. Again, they try to tie these  
9 questions of your back problems and how are you  
10 living both physically and socially and mentally.  
11 A very common form of outcome measure  
12 is the SF-36 or Short Form 36, 36 questions meant  
13 to evaluate your health in two overall domains,  
14 physical health and mental health, with four  
15 domains within each one, and the physical health  
16 domain within the SF-36 includes a pain component,  
17 but that's two questions about pain.  
18 And then other studies seem to have  
19 adopted some other types of scales which again,  
20 the properties of are difficult to assess in  
21 relation to this specific procedure. It's very  
22 complicated, I don't know if we can -- we'll just  
23 kind of have to take what the studies tell us and  
24 have the experts inform us as to the properties  
25 and abilities of those scales to tell us

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1 meaningful information. So this is just an  
2 introduction, it's a very complex field, and I'm  
3 far from an expert on each of these individual  
4 scales.  
5 So in terms of the nature of the  
6 question, what are the effects of vertebroplasty  
7 for osteoporosis-associated fractures, these are  
8 people with fragile bone that's collapsed versus  
9 those that have a malignant process which has made  
10 the bone fragile. And what we found mostly is  
11 case series studies, that's the predominant form  
12 of study out there, and later on I'll review the  
13 comparative studies that we found.  
14 But of those studies that met our  
15 criteria, we found 11 case series studies with a  
16 total of over 900 patients. Varying sample size.  
17 And what we see is that there is a variable  
18 work-up and imaging evaluation for these studies,  
19 and I think the experts will be able to inform us  
20 on what the type of work-up is and what type of  
21 patients can be included and excluded, but it  
22 varies between studies, and so, they could inform  
23 us as to what the consensus is and whether  
24 different people would agree about who is a  
25 candidate for the procedure.



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1 My report has varied and detailed  
2 tables, and I'm trying to get out the major  
3 issues, and there is some more detail in the  
4 written report, but I will try to present it in an  
5 efficient fashion.  
6 But they vary in terms of the average  
7 symptom duration, so an important question for  
8 Medicare is the chronicity of the fracture. And  
9 so, since there were many studies that did not  
10 report the duration of both the fracture and the  
11 result of any kind of straightforward evaluation  
12 all the time, some of the studies included  
13 patients with only short-term duration, and one  
14 study with a long symptom duration. And then they  
15 also varied in the respect that they followed up  
16 the patients for their improvement, and you can  
17 see there is quite a range in how far out after  
18 the procedure the patients were followed.  
19 So, this is my attempt to take our very  
20 detailed tables and give you the broad brush  
21 stroke of the results based on the outcome of a  
22 one to ten visual analog scale or, to the best of  
23 our ability, to normalize whatever scale the  
24 investigator used to a one to ten scale. So if  
25 they used another visual analog scale that didn't

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1 used the maximum score ten, then we kind of scaled  
2 the others proportionately and hopefully that  
3 makes the studies comparable.  
4 But the studies that varied in their  
5 techniques for evaluating the pain, some were a  
6 multi-question, some is a one-question, and there  
7 might be variations, there are probably variations  
8 even in showing the patient a single scale or  
9 asking them a single question.  
10 But we can see among the case series  
11 studies that at baseline, the VAS scores at this  
12 range with ten being the maximum, anywhere from  
13 6.9 up to the nine-point-something. Some of these  
14 patients, you can imagine the question being, is  
15 this the worst pain you ever felt? And several of  
16 the studies only evaluated, four of the studies  
17 here only evaluated the patients right after the  
18 procedure, but we can see that there was relief  
19 down to 1.9 to 3.7, and I didn't put a statistical  
20 significance because within the context of these  
21 studies and their reasonable sample sizes, the  
22 changes of this magnitude are all statistically  
23 significant, so you can assume that almost  
24 everything I'm pointing out to you here is  
25 statistically significant. So several studies

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1 just evaluate the procedure right after and then  
2 they don't keep track of the patients after that.  
3 And then three studies which evaluated the  
4 patients from one month to six months, and again,  
5 you can see that there is still a decrease from  
6 baseline. And there were some studies that  
7 evaluated at a year and further out. Again, these  
8 are single case series studies with no control arm  
9 in the study.  
10 What's not noted here is that some of  
11 these studies have some losses to follow up, so  
12 they aren't able to fully, they don't have their  
13 full number of patients at the end of the study,  
14 that's in my detailed report. Half of the  
15 studies, or about half the studies probably had  
16 fairly thorough follow-up. I think the studies  
17 that really lost track of half of their patients,  
18 they were not included in our report.  
19 These are the studies that looked at  
20 other outcome measures and as I said, it's hard to  
21 know the exact properties of these measurements  
22 and even if they are well known for other  
23 patients, they may not be well known for these  
24 specific type patients, so we just kind of have to  
25 accept the scale for what it tells us and kind of

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1 have a gestalt about what the magnitude of the  
2 difference is. But we can see some studies used  
3 some ordinal scale for mobility and some ordinal  
4 scale for pain medications. The Oswestry score in  
5 this particular study, they scaled it from one to  
6 five versus one to a hundred, so this is the more  
7 common ways that the Oswestry scale, everyone went  
8 from 70-something percent down to 16, so a big  
9 difference, and then some studies using measures  
10 of quality of life on the ordinal scales.  
11 These studies had various methods of  
12 showing their complication rates, and the most  
13 common being cement leak, so these are the rates  
14 of anatomic cement leak as noted on either CT scan  
15 or plain x-ray according to the method of the  
16 author. And we can see that cement leaks are  
17 common, but less common are symptoms associated  
18 with those leaks, and then commonly these studies  
19 will have a notation about specific patients that  
20 had a more severe neurologic type problem. And  
21 then some studies showed in a rather nonsystematic  
22 fashion the frequency of new fractures at a  
23 certain time after the procedure.  
24 We did the same type of review for  
25 malignancy-associated fractures for vertebroplasty

00029

1 and I will just go over those quickly. Again, a  
2 smaller number of studies, three case series  
3 studying a total of 70 patients. If we look at  
4 the visual analog scale, the results in  
5 termination of pain from baseline compared to  
6 follow-up and the magnitudes of the change seemed  
7 to be similar to that for the osteoporosis  
8 patients.  
9 Now we found one published  
10 nonrandomized comparative trial comparing  
11 vertebroplasty to conservative treatment, and so  
12 this study I will review in a little more detail.  
13 These patients all had evidence of acute fractures  
14 so they had not had a whole lot of time to see if  
15 they would get better, and they were all evaluated  
16 and they either agreed to have the vertebroplasty  
17 or they agreed that they wanted to have  
18 conservative treatment. And the results of the  
19 study, to quickly sum up, in the vertebroplasty  
20 group, their pain level at baseline was 19 and  
21 then within a day of the procedure it went to nine  
22 and then to five and then to four for long-term  
23 follow-up. But the control group, they of course  
24 had no pain relief after one day, but within six  
25 weeks the difference between the vertebroplasty

00030

1 and the control groups were no longer significant.  
2 The Barthel index, which is a measure of function,  
3 showed similar findings, some pain relief within  
4 one day, but within six weeks and at six and 12  
5 months, there was no difference between the two  
6 procedures.  
7 Dr. Kallmes had a pilot trial, a sham  
8 controlled study, and I don't have slides of  
9 these. They were two randomized trials that have  
10 only been reported in the abstract form, so I  
11 don't have slides of those. But these are not  
12 published because we -- I will report them because  
13 they report randomized controlled evidence, but we  
14 only have minimal reporting of these findings.  
15 So, Dr. Dohm did a study of 31 patients  
16 and among those patients, they were randomized to  
17 either immediate or delayed vertebroplasty, and  
18 among the patients who had the vertebroplasty  
19 first, they did have some pain relief from an  
20 average value of 9.4 to 3.3 after the procedure.  
21 And the medical therapy procedures did not have  
22 any relief after six weeks of conservative  
23 treatment but after their vertebroplasty they did  
24 have some improvement.  
25 And then Dr. Kallmes did a small pilot

00031

1 study, I hope I'm quoting the results of that  
2 pilot study correctly. This was a very small  
3 study with about five patients who had a  
4 sham-controlled procedure, and he might be able to  
5 describe the nature of the sham better. But among  
6 patients who were initially treated with the sham  
7 procedure, they had minimal relief after  
8 treatment, they crossed over to vertebroplasty,  
9 but then the results after vertebroplasty were  
10 similar. Both patients who initially underwent  
11 vertebroplasty and had minimal relief in symptoms,  
12 and crossed over to receive the sham procedure,  
13 and one of these patients reported complete relief  
14 after the sham procedure.  
15 DR. MCNEIL: Dr. Mark, we're going to  
16 have to ask you to move along. You have two  
17 minutes.  
18 DR. MARK: Okay, let me move quickly.  
19 So, the results of this sham-controlled procedure  
20 raise issues about regression of the mean, placebo  
21 effect, the natural history of patients with this  
22 condition, and we found mostly the literature  
23 consisted of case series studies and there is a  
24 lack of randomized clinical trials in this field.  
25 So, the Blue Cross Blue Shield panel made a

00032

1 decision on reviewing this evidence that it did  
2 not meet our particular criteria as an effective  
3 procedure based on the type of evidence that  
4 exists for this procedure so far.  
5 I will try to spend, just quickly, the  
6 results are very similar for kyphoplasty patients  
7 in terms of the degree of pain relief that is  
8 achieved or that we see in the case series  
9 studies, so this is a quick view of the baseline  
10 versus the postoperative outcome for patients who  
11 receive kyphoplasty. And we see that there were  
12 seven case series studies, again, similar baseline  
13 pain scores, and a decrease in the VAS, visual  
14 analog scales, to one to two to three to four,  
15 whatever time period they were evaluated at. So  
16 again, mostly case series for kyphoplasty.  
17 Several of these studies measured some  
18 functional scales and most of these differences,  
19 again, scales are complicated, don't try to absorb  
20 it, but there were statistically significant  
21 improvements in these domains of quality of life  
22 and function.  
23 Cement leaks are much rarer, or the  
24 proportion that has cement leaks seems to be lower  
25 than for vertebroplasty. Malignancy, again,



00033

1 similar findings.  
2 We did find two nonrandomized  
3 comparative studies for kyphoplasty, one just  
4 published this month and the other only available  
5 in a foreign language publication for which we  
6 have I believe a reasonable translation, although  
7 I'm not sure. The difference in these  
8 observational studies was that in the Kasperk  
9 study, there were improvements in pain, whereas  
10 the control group does not change their pain  
11 scores. This is the most --  
12 DR. MCNEIL: Dr. Mark, can you wrap up?  
13 DR. MARK: Okay. And again, there were  
14 statistically significant improvements in the  
15 kyphoplasty group. The other German language  
16 publication shows similar findings, again, the  
17 contrast with the other observational studies in  
18 showing that the control group remained at the  
19 same pain level and the kyphoplasty group had  
20 improvement.  
21 So, in sum, we have mostly case series  
22 that are the predominant evidence, we have a  
23 relatively small number of nonrandomized  
24 comparative studies, and some randomized  
25 controlled trials in abstract form only, and only

00034

1 one sham-controlled but very small pilot study.  
2 Thank you.  
3 DR. MCNEIL: Thank you very much,  
4 Dr. Mark. Dr. Lieberman.  
5 DR. LIEBERMAN: Good morning. I would  
6 like to thank the MCAC panel for inviting me to  
7 present this morning. It's an honor to be here in  
8 front of a distinguished and esteemed audience. I  
9 would like to share with you some of the work that  
10 we have been doing at the Cleveland Clinic and my  
11 thoughts on vertebral augmentation as it relates  
12 to vertebroplasty and kyphoplasty.  
13 Just so that I'm complying with the  
14 disclosure mechanism, I do have consulting  
15 arrangements with each one of these listed  
16 companies and I have received grant and research  
17 support from each one of these companies.  
18 I have had the privilege over the last  
19 eight years of working with a spectacular team.  
20 We have had a number of fellows, residents,  
21 clinical staff and interesting individuals who  
22 have worked with us on this project of vertebral  
23 augmentation. As a summary, we have now had 12  
24 peer reviewed publications in the literature, four  
25 peer reviewed publications that are currently in

00035

1 print, two that are in review, six letters and  
2 editorial comments, and 14 book chapters. I am  
3 absolutely indebted to these individuals for  
4 working above and beyond to try to do the science  
5 right.  
6 You're going to hear an awful lot today  
7 about vertebral compression fractures. There's a  
8 lot that we do know, there's a lot we don't know,  
9 and the way I like to look at it is that the glass  
10 is three-quarters full or one-quarter empty, and  
11 I'd hate to pour out the three-quarters full glass  
12 because it's only one-quarter empty. Right now we  
13 know that two-thirds of these compression  
14 fractures are undetected and eventually become  
15 pain-free, one-third become chronic.  
16 Why? We don't know, is it because of  
17 true pseudoarthrosis, because of altered  
18 biomechanics, because of osteomalacia, or some  
19 other unknown reason. But I can put forward to  
20 the panel that once that vertebral body collapses  
21 down, not a single one of those vertebral bodies  
22 ever regains its normal height, nor does the spine  
23 regain its normal sagittal alignment, unless of  
24 course we intervene.  
25 Today in orthopedics, we would never

00036

1 even dream of leaving Granny in bed with a broken  
2 hip, we know the problems associated with that.  
3 We would never dream of leaving a wrist or an  
4 ankle fracture in a malunited, in a  
5 physiologically or biomechanically compromised  
6 situation. Well, why in the spine up to now have  
7 we been content to leave these vertebral bodies in  
8 a biomechanically and physiologically compromised  
9 position? Because we haven't had good treatments  
10 up to now. Surgical repair has been invasive and  
11 these patients are vulnerable; they have multiple  
12 comorbidities and surgery was a major undertaking  
13 with very poor outcomes.  
14 I would like to spend a few minutes  
15 just talking about the biomechanics of the spine.  
16 Load transfer through the vertebral bodies is a  
17 very complex phenomenon. If you've got a normal  
18 vertebral body, the normal vertebral body on the  
19 left-hand side of the screen, if you load it, what  
20 you see is up to 80 percent of that load is  
21 transmitted through the center of that vertebral  
22 body, whereas but 20 percent of that load is  
23 transmitted through the compact cancellous shell  
24 surrounding the body. On the other hand, if  
25 you've got an osteoporotic bone and you load that

00037

1 bone, far less of that force can transmit through  
2 the bone and what happens is you transfer that  
3 force through that shell anteriorly and  
4 surrounding it to get down to that next vertebral  
5 body. So we see a force transmission issue  
6 through that vertebral body.  
7 So the spine then becomes like the  
8 leaning tower of Pisa. If you've got a crack in  
9 the bone but you've got physiologically normal  
10 bone, that bone will heal. The crack may settle a  
11 little bit, but will not collapse down any  
12 further. If on the other hand you've gone an  
13 osteoporotic or an osteolytic process, the spine  
14 continues to collapse. The resulting bone edge is  
15 exaggerated and what you see is forced  
16 concentration at that index level. Well, the  
17 physiologic process doesn't get any better, but  
18 the leaning tower of Pisa keeps leaning, and what  
19 we now see is force transmission to the vertebral  
20 body or the bone below, to that vulnerable  
21 anterior cortex where because that center of the  
22 vertebral body above is deficient, you have more  
23 force concentration, so kyphosis begets further  
24 kyphosis.  
25 Dr. Mark Kayanja is one of my fellows

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1 and is now on staff at the Cleveland Clinic. He  
2 just successfully defended his Ph.D. thesis, a  
3 culmination of four years of work looking at all  
4 of this information. And what we've done is look  
5 at the strain distribution above and below, look  
6 at prophylactically augmented vertebral bodies,  
7 look at the strain distribution after a fracture,  
8 look at the biomechanical effect of varying  
9 different numbers and different levels of cement  
10 augmentation, and he has created a very elegant  
11 model for looking at all of this, and he's come up  
12 with significant conclusions that really do mirror  
13 what we see clinically, and we were able to look  
14 at that in the lab and verify the effects of what  
15 we are doing with respect to our intervention.  
16 He found that the strain is  
17 concentrated at the apex of the curve, the forced  
18 concentration. The superior adjacent vertebra is  
19 at higher risk of subsequent fracture, which is  
20 exactly what we see clinically. Cement  
21 augmentation normalizes the load transmission  
22 through that vertebral body, so if you put a block  
23 of cement in the middle, you infiltrate that  
24 vertebral body, you are no longer transmitting the  
25 force through the cortex, you're normalizing the

00039

1 load transfer. Increasing the centrum load  
2 transfer from augmentation reduces the stiffness.  
3 Now, there is a lot of confusion in the  
4 literature about these terms, stiffness and  
5 strength. The stiffness is a function of the  
6 surrounding bone so as you continue to load it  
7 beyond physiologic loads, that bone is still going  
8 to compress, but that cement block is going to  
9 transmit the force. And then while we increase  
10 the number of levels, the segmental stiffness and  
11 strength is maintained. That just proves that we  
12 are protecting the spine in the upright position.  
13 So all of these conclusions are now the  
14 basis of three papers, two of which are already in  
15 print, one is in press, and a multitude of papers  
16 that are currently being prepared or in review.  
17 So we've got this spectrum of vertebral  
18 augmentation from vertebroplasty to kyphoplasty,  
19 and we're looking at stabilization, reduction or  
20 formal reconstruction, and these treatment methods  
21 should not be considered mutually exclusive.  
22 These are tools in our toolbox that we should pull  
23 out of the toolbox and use at the most appropriate  
24 time in the treatment of these osteoporotic and  
25 osteolytic compression fractures.

00040

1 I would like to share with you now some  
2 of the work that we've been doing clinically at  
3 the Cleveland Clinic. I have now had the  
4 privilege of treating over 500 patients from April  
5 '99 to the present. Again, I'm indebted to my  
6 clinical staff for helping collect these data and  
7 being religious in the follow-up, driving the  
8 patients home and bringing them in for x-rays, and  
9 all sorts of things like that. We did a  
10 prospective cohort study, we planned things ahead  
11 of time, we used given objective validated outcome  
12 scores and did all the statistical analysis. Two  
13 of our papers have already been quoted; we've got  
14 a third paper which is now in review with  
15 Osteoporosis International.  
16 What I'm going to show you is the work  
17 we've done analyzing 329 of these patients, of  
18 which about 70 percent were osteoporotic patients,  
19 25 percent were myeloma patients, and we had a  
20 number of other malignancies. We have performed  
21 917 kyphoplasties in these patients. If you look  
22 at the spectrum of vertebral bodies that I've  
23 treated, it goes all the way up and down the  
24 spine, but again as we know clinically, it's at  
25 the thoracolumbar junction that is the vulnerable



00041

1 area. Our mean follow-up is about 55 weeks. The  
2 duration of symptoms in this group was anywhere  
3 from one week to five years. 93 percent of these  
4 patients underwent general anesthesia, seven  
5 percent underwent local anesthetic, and the  
6 average hospital stay in this group was 1.1 days.  
7 Now this is probably the most important  
8 slide. This is our whole group, N=329. We had  
9 full information on 72 percent but the analysis  
10 was done with an intent to treat. This is the  
11 SF-36, these are the combined scores on the SF-36  
12 and the Oswestry disability. The white bars  
13 represent age-matched controls, so 70-year-old  
14 North Americans with no comorbidities. And you  
15 can see statistically significant improvement in  
16 bodily pain, in mental health, in the raw  
17 emotional score, the physical function score, the  
18 social functioning and vitality, as well as  
19 improvements in their Oswestry disability score.  
20 So I have no doubt that we are  
21 intervening and we are changing the natural  
22 history. We are showing that these patients are  
23 better, and you're going to hear a lot more about  
24 the natural history of compression fractures and  
25 the function of our patients as they get going.

00042

1 We broke it down. We have done this analysis a  
2 dozen ways.  
3 So now we took minimum 12-month  
4 follow-up, 94 patients, again, complete  
5 information on these 94 patients in an intent to  
6 treat analysis, statistically significant  
7 improvement across bodily pain, physical function,  
8 role function, social functioning and vitality in  
9 that group.  
10 We did one with a minimum 24-month  
11 follow-up, 48 patients. Again using an intent to  
12 treat analysis, looking at these, there is a  
13 statistically significant improvement in bodily  
14 pain, physical function, social function and  
15 vitality.  
16 We move on to just the osteoporosis  
17 now, so we pulled out only the osteoporosis  
18 patients. 73 percent follow-up, similar trend,  
19 approaching age-matched control with statistically  
20 significant improvements pre and post-op.  
21 We looked at our myeloma patients. 80  
22 patients, 76 percent follow-up, very similar  
23 trends. We are making a difference in their pain,  
24 in their function, in their vitality in this  
25 compromised patient group.

00043

1 And then here is the tumor group, and  
2 this would be one area that we're a little  
3 deficient. We only have 21 patients and a lot of  
4 these were palliative procedures. We don't have  
5 as good of follow-up, only 66 percent, and you can  
6 really only see three areas, physical function,  
7 social function and vitality, where we made or  
8 showed a statistically significant improvement.  
9 But overall, we have documented that these  
10 patients do well after this intervention.  
11 The next issue is the vertebral height  
12 restoration. In one of our initial papers we  
13 showed that on average we were able to restore  
14 about 47 percent of the height lost. That was  
15 early on, that was before I really understood a  
16 lot of the subtleties of vertebral compression  
17 fractures.  
18 We have now got a study that is still  
19 ongoing, although the initial results have been  
20 published in abstract form, 23 patients, single  
21 level osteoporotic vertebral compression  
22 fractures, new patients coming in, one level. We  
23 look at their pre-op x-rays, we compare them to  
24 the prone position x-rays after we inflate the  
25 balloon, after we deposit the cement, and then

00044

1 post-op standing x-rays. And you can see that  
2 there is a significant improvement from post-op  
3 standing at 11 millimeters. There is a positional  
4 effect. When we put these patients on the table  
5 we do get a hyperlordotic moment, we do get some  
6 passive correction. When we place (inaudible)  
7 another four millimeters correction. When we  
8 deposit the cement, we are able to maintain it.  
9 They stand up on average with the measures that we  
10 get, 11 millimeters of height improvement.  
11 The complications, and some of my  
12 papers were reported in the first talk, we had far  
13 less than ten percent cement extravasation, most  
14 of these through little fissures in the end plate  
15 or through the sidewall, and we've developed  
16 techniques to try to minimize that. In this group  
17 of patients we have had absolutely no neurologic  
18 complications. We've had no acute infections, but  
19 I do now have three patients that presented with  
20 latent infections, two of which were  
21 neurocompromised tumor patients, one of which was  
22 a very debilitated elderly woman. All of these  
23 presented more than six months out after the  
24 procedure.  
25 The issue of subsequent remote and

00045

1 adjacent level fractures, that's a big issue and  
2 intuitively one would think if you're going to put  
3 a block of cement in the spine, you're going to  
4 change or alter the biomechanics, you're going to  
5 generate other fractures. Well, we set out to  
6 look at exactly what our incidence was. We looked  
7 at 115 patients and saw that in that 115 patients,  
8 26 of them had 33 fractures, but we quickly  
9 realized this was a mixed bag. If we took out the  
10 primary osteoporotic patients, we saw that they  
11 only had an 11.25 percent rate of remote or  
12 adjacent level subsequent fracture. If you looked  
13 at the osteoporotics due to steroids, we saw that  
14 they had a 45 percent rate, two separate animals.  
15 So we've got to go back to that natural  
16 history; Lindsay reported a natural history of  
17 about 19 percent after your first compression  
18 fracture. So if we look at our osteoporotic  
19 group, we are about half of the natural history,  
20 with biomechanics, restoring the alignment of  
21 these patients. I still don't know why in our  
22 patients with secondary osteoporosis the rate is  
23 so high. I suspect it's because it's a younger  
24 population that is more active, you fix their one  
25 fracture and they go out and feel they can shovel

00046

1 snow again without taking care of the rest of  
2 their bone problems.  
3 So we can go through the literature,  
4 and this literature is going to be harped on over  
5 and over again, but I just wanted to point out a  
6 couple things. Dr. Ledlie's paper, the visual  
7 analog score went from 8.6 to 1.4; height  
8 restoration, 66 percent to 85 percent.  
9 In Dr. Phillips' paper he had visual  
10 analog scores rating pain relief from any type  
11 kyphotic correction of 14 percent, remote or  
12 adjacent level fracturing, nine percent, very  
13 consistent results.  
14 This is a paper that was alluded to  
15 earlier by Majd, which has just recently been  
16 published in Spine Journal. 360 kyphoplasties on  
17 222 patients. Mean height restoration, 50  
18 percent, a 12 percent adjacent or remote level  
19 fracture, and median pain relief in about 90  
20 percent of these patients. Again, large series,  
21 independent series, very consistent results.  
22 This is the paper that we alluded to  
23 earlier, Komp's paper looking at 19 kyphoplasties  
24 versus 17 patients that were treated  
25 nonoperatively. The results, you can see the

00047

1 kyphoplasty results out to 24 weeks. The visual  
2 analog scores improved considerably and  
3 considerably in the nonoperative group, the visual  
4 analog scores deteriorated. Oswestry Disability  
5 improved considerably, in the nonoperative group,  
6 deteriorated considerably. So they conclude that  
7 kyphoplasty is superior to nonoperative treatment  
8 for these vertebral compression fractures.  
9 Here is a typical example. This was an  
10 82-year-old male who presented to me in September  
11 of 2000 after cutting down trees in his back yard  
12 and moving around, he had typical back pain. You  
13 can see the 12-millimeter loss of height, kyphosis  
14 of 23 degrees, and you can now see after the  
15 vertebral augmentation, it restored the height to  
16 29 millimeters, with kyphosis of 8 degrees. Now  
17 by no means is this perfect, but this is certainly  
18 better than when he started out.  
19 If we go to the vertebroplasty  
20 literature, there are a lot of good papers out  
21 there that show, again, that vertebral  
22 augmentation does make a difference.  
23 Here's a paper by Evans reporting on  
24 488 patients. Duration of pain was two weeks to a  
25 year. They analyzed this with a telephone

00048

1 interview at seven months and the pain score which  
2 was 8.9 before had improved to about 3.4.  
3 This is Grados's paper, and the reason  
4 I put this up is to show the difference, again,  
5 biomechanically in the spine. They reported a 52  
6 percent remote and adjacent level fracture rate  
7 and I believe that that's because of the  
8 biomechanics and the realignment issues which  
9 would not be addressed with this technique.  
10 Here is Amar's paper looking at  
11 ambulation. Again, 51 percent of their patients  
12 improved. Quality of life, 74 percent improved.  
13 Here is Hiwatashi's paper looking at  
14 positional height restoration average of 2.2  
15 millimeters, but when you look at 39 of their  
16 patients, it was greater than 3 millimeters, but  
17 there are difficulties in these measurements.  
18 And here's McKiernan et al's paper  
19 looking at their height restoration, and the  
20 important thing here is they report an 8.4  
21 millimeter height restoration from positioning  
22 with a kyphosis restoration of about 10 degrees.  
23 So in good hands, qualified hands, you  
24 can get very, very good results with these  
25 vertebral augmentation techniques.



00049

1 So what are the indications? Well,  
2 just like anything in spine surgery, patient  
3 selection is absolutely critical. These  
4 procedures are indicated for patients with  
5 progressive painful osteoporotic or osteolytic  
6 vertebral wedge compression fractures secondary to  
7 osteoporosis primary, secondary osteoporosis,  
8 multiple myeloma, or lytic metastases.  
9 If you were listening closely you would  
10 have heard me say progressive first, and I think  
11 you can feel my bias towards biomechanics of the  
12 spine and spine deformity as opposed to pain.  
13 Granted, a lot of the pain will settle down.  
14 What are the contraindications? Well,  
15 as with any procedures, there are  
16 contraindications to the anesthetic; pregnancy;  
17 bleeding disorders; pain that's unrelated to the  
18 vertebral compression fracture, and we certainly  
19 do see that; various different fracture  
20 configurations; or it's technically not feasible.  
21 If you've got a complex fracture or fractured  
22 pedicles or facets. The issue of solid tumor  
23 still hasn't been resolved and you have to  
24 evacuate the solid tumors first. Allergies to the  
25 device or procedures, and patients less than 40

00050

1 years of age.  
2 I'm still troubled by the current trend  
3 of taking patients under 40 and being subject to  
4 this kind of treatment. Here is an example of a  
5 40-year-old construction worker who fell off a  
6 scaffold. He walked into the emergency room with  
7 this burst fracture configuration, was seen by the  
8 physicians and told you need this operation. He  
9 went and had this operation and in the recovery  
10 room it was noted that he was neurologically  
11 compromised. CT scan noted that and he was  
12 immediately rushed back to the operating room for  
13 a decompression. What I would like to pay  
14 attention to and unfortunately (inaudible)  
15 anterior of that vertebral body, look at the  
16 quality of that bone. Here he is six months later  
17 after the decompression. That bone in front is  
18 completely melted away. That was normal healthy  
19 bone and I suspect what has happened is that we  
20 have created an environment of osteonecrosis.  
21 This gentleman has not been done any service by  
22 our profession.  
23 So, why have there been no randomized  
24 controlled trials addressing vertebroplasty and  
25 kyphoplasty? Well, I have personally been

00051

1 involved in five attempts and to sum it up, it's  
2 lack of collaboration. We haven't been able to  
3 get the various factions together to decide how to  
4 do the study or even participate in the study.  
5 There have been studies with design issues and IRB  
6 issues. One study that I was potentially involved  
7 with demanded a sham procedure, and my IRB would  
8 not let me do a sham procedure. There have been  
9 various funding issues. Some of us have tried to  
10 garner funding from various national and federal  
11 agencies and we have been told because this isn't  
12 (inaudible) or because there aren't other things  
13 or other conflicts, we do not get funded. But the  
14 last and probably the most important is the  
15 recruitment issue. We're dealing with an elderly  
16 population who don't have the time or the patience  
17 to come back for all these follow-ups and to fill  
18 out all this paper work.  
19 So, what are the fundamental  
20 differences? I don't think there are significant  
21 differences in terms of the pain relief outcomes,  
22 but in terms of the biomechanics, the techniques,  
23 the skill sets required, these are two different  
24 procedures which are associated with different  
25 skill sets and different work. There are issues

00052

1 of indications, issues of timing, the  
2 biomechanics, the number of levels, the void  
3 filler, and the physiology of the spine. I think  
4 that the risks are minimal in both these  
5 procedures, but we have to remember that the  
6 consequences may be substantial.  
7 And with that, I would like to thank  
8 you very much.  
9 DR. MCNEIL: Thank you very much,  
10 Dr. Lieberman. Why don't we have the panel for  
11 the next five minutes or so pose questions to  
12 Dr. Lieberman and/or Dr. Mark, and these would be  
13 questions for clarification. Are there any  
14 questions?  
15 DR. JARVIK: I have one small comment  
16 and then one clarification I would like to ask  
17 for. You referred to the series of patients that  
18 you collected as a cohort and in general I think a  
19 cohort requires a control group, and I don't think  
20 you had a control group in this series of patients  
21 that you collected and reported on. It's a small  
22 point but I think an important point.  
23 Just as a clarification, you mentioned  
24 that you analyzed this with intent to treat. What  
25 do you mean by that? That's usually, I think,

00053

1 reserved for randomized trials.  
2 DR. MARK: I am not a statistician. We  
3 do have statisticians at the Cleveland Clinic and  
4 as well as Johns Hopkins who have collaborated  
5 with this. I don't know the exact definition of a  
6 cohort. My interpretation of a cohort is a group  
7 of patients. This group of patients were  
8 prospectively defined and followed consistently,  
9 so that represents the cohort.  
10 With respect to the control, these  
11 patients acted as their own control because we had  
12 a pre-op, pre-intervention baseline on each one of  
13 these patients. The analysis of intent to treat  
14 was done according to what the statisticians  
15 explained to me. As we did not have complete data  
16 on these patients, they were considered failures  
17 in that, and the statisticians have various  
18 methods to address the deficiencies in the data by  
19 various averages and what have you, so it was as  
20 if they did not do well within that cohort.  
21 DR. MCNEIL: Yes, Dr. Weinstein.  
22 DR. WEINSTEIN: Thanks for your  
23 presentations, a lot of work in a very hard area  
24 to do. Likewise, I think that intent to treat is  
25 probably a misuse there. I think intent to treat

00054

1 means that you had some people that were intended  
2 to have nonoperative treatment or referred for  
3 some other treatment and they got that, versus  
4 those who were intended to have the intervention  
5 and got that. You can do an intent to treat  
6 analysis in an observational cohort but you need  
7 some comparative group. Did you have some  
8 patients who refused the procedure potentially who  
9 you followed? And second of all, what was the  
10 average age of your patients?  
11 DR. LIEBERMAN: We didn't have a  
12 nonoperative group that we consistently followed.  
13 And again, I left that definition up to the  
14 statisticians to develop, who again, were  
15 independent and not involved in any of the  
16 collection of the data, and that was their  
17 description to me of how to present this  
18 information.  
19 The average age of the entire group was  
20 73 years of age, I believe, I can't remember that  
21 slide, I can pull it up and get you the exact  
22 number, but that was the whole entire group. In  
23 the myeloma group the average age was a little bit  
24 younger than that but the osteoporosis group was  
25 found out to about 77.

00055

1 DR. WEINSTEIN: And in patients who  
2 refused treatment, did you follow those?

3 DR. LIEBERMAN: I still follow them in  
4 my clinic. I must say, I don't recall very many  
5 patients that refused treatment. We do have a  
6 very large practice and it's standard that all  
7 patients are followed in combination with our own  
8 operative spine physicians and our osteoporosis  
9 specialists and myself, but we haven't been  
10 documenting their outcomes.

11 DR. MCNEIL: Dr. Ondra.

12 DR. ONDRA: Dr. Lieberman, you  
13 emphasized spinal alignment and biomechanics.  
14 There's also a lot of discussion both in your talk  
15 and the literature regarding people with height  
16 restoration to a more limited degree, local  
17 (inaudible) correction. Is there any data that  
18 discusses the actual sagittal realignment, the  
19 question of the levels adjacent to, regional as  
20 well as global sagittal alignment.

21 DR. LIEBERMAN: Yes, there is data but  
22 the data is not significant at this point. The  
23 error of measurement in three-foot scoli films was  
24 just too difficult. We tried to monitor that, we  
25 took hundreds of x-rays trying to find the T2

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1 vertebral body versus the T12, and the quality of  
2 the x-rays and the angle of them just made it too  
3 difficult. We are now looking at using one of the  
4 quantitative deck scanners to look at overall  
5 alignment with that, but the problem is the  
6 patients are lying down to get that study so that  
7 doesn't help us at all either, it does help us  
8 with other fractures. It's a difficult area and  
9 we're looking for other ideas and if you guys have  
10 any suggestions as to how you think I can do this,  
11 I'm wide open, but it really is a tough thing.  
12 DR. MCNEIL: Dr. Resnick.  
13 DR. RESNICK: I would like to have some  
14 input from you guys as to what the differences  
15 were between the Diamond study and the Komp study,  
16 and I haven't had a chance to read the Komp study  
17 since it just came out, but it seems that the  
18 Diamond study seems to have a comparison looking  
19 at vertebroplasty and they didn't really notice  
20 much of a long-term effect. It was really more of  
21 a short-term effect because a control group which  
22 refused treatment got better after about six weeks  
23 or three months, whereas in the Komp study it  
24 didn't get better. Do you have any insight as to  
25 what the differences between those two control



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1 groups are?  
2 DR. LIEBERMAN: I don't know, either  
3 investigation studies or those two papers --  
4 DR. MCNEIL: Dr. Mark, do you have a  
5 comment on that?  
6 DR. MARK: Yeah. Let me try to  
7 remember some of the details. Now both of those  
8 studies, the difference between the Komp, the Komp  
9 study was a kyphoplasty study, an observational  
10 study to my recollections, and I might have to dig  
11 into the papers a little bit, but those patients  
12 had acute fractures. The Diamond study was a  
13 study of vertebroplasty, they also had acute  
14 fractures, and here's where the workup is kind of  
15 critical.  
16 The Komp study had some issue and  
17 again, this is a translation from the German about  
18 active fractures, mobile fractures and some kind  
19 of imaging study that was done, so they may have a  
20 slightly different subgroup of acute fractures.  
21 And again, that is my memory, kind of gleaning  
22 what the differences between these two groups of  
23 acute patients, but there seemed to be some  
24 additional criteria in that German Komp study.  
25 DR. MCNEIL: So this, I guess going

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1 back to I guess Dr. Jarvik's point, would talk to  
2 the issue of a control group, if we're not  
3 entirely clear how the subsets differ from one  
4 population to another.

5 DR. MARK: Yeah, I think one study uses  
6 slightly different criteria, and some of the  
7 studies focus on issues which you're an expert on  
8 about mobile fractures, and I imagine that means  
9 something that you can see move on a different  
10 dynamic mobility and imaging, and other studies  
11 seem to not address that as a criteria.

12 DR. MCNEIL: Dr. Fessler.

13 DR. R.G. FESSLER: I have a question  
14 for Dr. Mark. I'm confused about your conclusion  
15 and maybe you can clarify it for me. It seems to  
16 me that you reviewed prospective data but not  
17 randomized controlled data for several thousand  
18 patients, and then on the basis of one study made  
19 the conclusion that we're not able to assess the  
20 technology, primarily because those other studies  
21 are not controlled or randomized and the small  
22 study was. That seems to deny the sniff test, you  
23 know, the obvious benefits this has to the  
24 patients in the six months they're enduring severe  
25 pain, and if you look at the six-month or one-year

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1 data, their pain seems to be normalized. It seems  
2 to me you're making a conclusion that we can't  
3 assess the technology after reviewing thousands of  
4 patients that it seems so effective on.

5 DR. MARK: I think our conclusion was  
6 based, not that the randomized controlled trials  
7 are definitive evidence of no benefit, but that  
8 the deficiencies of some case series studies, and  
9 again, sometimes they can be believed. But these  
10 patients, there is no control group and each  
11 patient is their own in-flight control in a case  
12 series study. But again, due to the selection  
13 criteria, the natural history of patients who have  
14 gone through the selection process may not be as  
15 well defined. But I think the issue is, do these  
16 case series kind of give us reliable evidence of  
17 efficacy without control groups? Yes, these  
18 patients did get better, but is that definitive  
19 evidence of efficacy in the group?

20 DR. MCNEIL: I'll just say a word here.  
21 I think what the Blue Cross groups do is pay  
22 special attention to the U.S. Preventive Services  
23 Task Force on Quality of Evidence, as well as to  
24 the Cochrane collaboration's criteria on quality  
25 of evidence. When both of those sets of criteria

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1 are looked at, the randomized clinical trials  
2 obviously come out on top and case series, cohort  
3 studies where a definable controlled group can be  
4 easily identified fall down a little bit, and I  
5 think that's what Dr. Mark is saying.  
6 I think we're probably going to have to  
7 move on, but I would just like to ask, as I took  
8 one quick look at the Cleveland Clinic experience,  
9 you say you had a very large osteoporotic clinic.  
10 Can you tell me how many acute fractures or how  
11 many patients who may be eligible for this  
12 procedure you would see there in a year?  
13 DR. LIEBERMAN: I don't know the  
14 quantity of patients that come to our clinic, but  
15 we have 13 regional satellite hospitals, we've got  
16 six osteoporosis specialists and five nonoperative  
17 spine specialists, and they all see that volume of  
18 patients. I can tell you in the surgical group,  
19 we are doing probably close to 250 vertebral  
20 augmentations a year, and then we have our  
21 anesthesia group and our radiology group who are  
22 also doing vertebral augmentation, they probably  
23 add another 50, so we're talking about 300  
24 patients a year that come through the Cleveland  
25 Clinic that get vertebral augmentation, but I

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1 don't know the total population.  
2 DR. MCNEIL: So, the question I was  
3 getting at, what fraction of that is the total and  
4 how do we know the characteristics of that related  
5 to the operation group?  
6 DR. LIEBERMAN: I don't know the total.  
7 I know the symptomatic ones do get sent, there is  
8 a triage mechanism in place right now.  
9 DR. MARK: There is one other study  
10 that we reviewed, a Kasper observational trial  
11 that actually looked at all the patients that they  
12 evaluated to enter the trial, that met their  
13 original entry criteria and eventually went on to  
14 be either eligible for the procedure or the  
15 observational arm, and they estimated with  
16 patients with fractures and pain and some  
17 disability, about 50 percent of those patients  
18 were deemed anatomically and through other kinds  
19 of indications to be eligible for either the  
20 observational trial or their intervention arm.  
21 DR. MCNEIL: Great, thank you for that  
22 clarification. Why don't we move on to Alabama.  
23 Moving south, Dr. Saag and Dr. Bian, are you both  
24 speaking, or dividing it, or how is that working?  
25 DR. SAAG: Thank you very much. Good

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1 morning. It's a pleasure to be here. I am a  
2 rheumatologist and outcomes researcher, and also  
3 an osteoporosis specialist. I spend part of my  
4 time seeing patients with real-life fractures.  
5 It's a pleasure for me also to acknowledge the  
6 support that we received through the Agency for  
7 Health Care Policy and Research, the group that  
8 supports our Center for Education and Research on  
9 Therapeutics. We're one of seven centers funded  
10 by AHCPR to look at the safety and effectiveness  
11 of drugs, devices and biologics.  
12 What I'm going to do is follow in the  
13 theme of the other speakers and comment briefly  
14 about the natural history of osteoporosis as it  
15 pertains to the vertebrae, talk a little bit more  
16 about some of the evidence and our interpretation  
17 of this, and particularly highlight where we see a  
18 major gap in the evidence, and then use that as a  
19 segue to talk about a study that we're doing right  
20 now in collaboration with Blue Cross and Blue  
21 Shield and with the FDA looking at vertebroplasty.  
22 So I think to back our discussion up  
23 just a little bit and highlight the public health  
24 implications of vertebral compression fractures,  
25 we've heard already about some of the significant

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1 consequences, the fact that many of these  
2 fractures are silent and do not present clinically  
3 as very important, and hesitation in terms of  
4 doing studies that appropriately identify and  
5 follow these people longitudinally. We've heard  
6 about height loss, and there are other  
7 consequences of vertebral compression fractures  
8 that listed here, which are indeed significant.  
9 The effects on daily living activities  
10 are truly important but it has also become  
11 realized that not only do we need to worry about  
12 morbidity of vertebral compression fractures, but  
13 there is also a higher risk of all-cause  
14 mortality, bearing in mind that oftentimes this is  
15 a harbinger for other comorbidities and a  
16 predictor of other disease states.  
17 This is some data that highlights the  
18 likelihood of developing a subsequent vertebral  
19 compression fracture based on results of the  
20 control arms of a number of randomized clinical  
21 trials looking at a variety of different  
22 osteoporotic therapies and also cohort analyses.  
23 And you can see that not only does vertebral  
24 compression fracture denote a much higher risk of  
25 having a subsequent event, a figure of 19 percent

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1 or 20 percent was used earlier as the likelihood  
2 of fracture in the next year, but there's also a  
3 higher likelihood of having fractures at other  
4 sites, particularly in the hip, where we know  
5 there is a very substantial morbidity and higher  
6 mortality.  
7 Well, this data is perhaps somewhat  
8 surprising. This is work by John Kanis and  
9 colleagues looking at a group of patients in  
10 Sweden, and showing that although we normally  
11 think about hip fractures as having the highest  
12 attributable mortality, it was actually vertebral  
13 compression fractures that seemed to look a little  
14 bit worse in following people longitudinally over  
15 time.  
16 And lest we forget, there are other  
17 therapeutic approaches to osteoporosis, and that  
18 surgical approaches, while potentially effective  
19 in restoring height and relieving pain acutely,  
20 have some issues that we have been discussing  
21 today and will discuss further. There are a  
22 variety of medical therapies that have been tested  
23 in a variety of large randomized clinical trials  
24 and this is just a non-head-to-head comparison of  
25 the variety of therapeutic agents ranging from



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1 Raloxifene to Teripartide, showing the level of  
2 relative risk reduction that can be achieved among  
3 women that have had at least one fracture, and  
4 this is looking at the development of the  
5 secondary event. And you can see a range in  
6 relative risk reduction ranging from 30 to 65  
7 percent across studies that are really not  
8 comparable. We're looking at different inclusion  
9 criteria, even different definitions of how  
10 vertebral compression fractures are defined within  
11 these populations. And we get the sense that with  
12 some limitations on study design that there are a  
13 variety of therapeutic options that seem to be  
14 effective in attenuating the risk of subsequent  
15 fractures.  
16 When we begin to hear today extensively  
17 about vertebroplasty and kyphoplasty, and we have  
18 seen some pictures already of what the procedure  
19 looks like, it's interesting that it has not been  
20 available for that long in the United States, and  
21 it is a procedure that has been around longer  
22 internationally.  
23 This just provides a brief synopsis of  
24 kind of where we think we are with the literature  
25 at this point in time. It's also interesting to

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1 note that this was an off-label use of bone cement  
2 until very recently when the FDA approved the use  
3 of KyphX for this indication. And we have seen  
4 data already from our first two speakers  
5 highlighting the short-term to moderate-term pain  
6 relief from the restoration of vertebral height  
7 that has been fairly consistently identified with  
8 both vertebroplasty and kyphoplasty. What we've  
9 also heard very loud and clear is that there is  
10 little evidence on long-term effectiveness and  
11 safety. It's also been highlighted in a recent  
12 editorial, there's been roughly 200 studies in  
13 this area, and we heard from our earlier speakers  
14 that there are only two RCTs that have been  
15 presented in abstract form. So mostly, we're  
16 focusing on observational data, we're looking at  
17 small observational studies that are occasionally  
18 comparative, but generally case series without  
19 comparison groups.  
20 We've also heard today about the  
21 potential complications and adverse outcomes, the  
22 short-term ones being bone cement leakage, a  
23 potential during the actual procedure, rib  
24 fracture, and then the potential procedurally  
25 associated issues of other forms of embolic

00067

1 applications.  
2 Where our interest is focused and what  
3 I will be discussing and Dr. Bian will be  
4 highlighting in terms of the study that's  
5 underway, are the long-term complications. What  
6 about the increase risk of adjacent fractures or  
7 secondary fractures after this procedure, as Dr.  
8 Lieberman began to address as well. And then also  
9 unknown is the subsequent risk of polymethyl  
10 methacrylate toxicity, particularly in this body  
11 location.  
12 So, I wanted to just highlight a couple  
13 of studies, and this is the Diamond study that has  
14 already been mentioned. I won't spend much time  
15 on this since it's been covered in some detail,  
16 but what I think is very intriguing about this  
17 study was the consistency with other earlier  
18 studies without comparative groups of the  
19 short-term improvement in symptomatic relief with  
20 pain being reduced substantially within 24 hours.  
21 However, as was highlighted at six weeks and then  
22 again at six and 12 months, it was very similar  
23 pain control.  
24 As we look at the data, and Dr. McNeil  
25 began to highlight this very issue, we see that

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1   there are different grades of evidence, and most  
2   of what we're dealing with in this field to date,  
3   again because of the challenges in doing RCTs of  
4   surgical therapies, the difficulties in this  
5   procedure being relatively new, are mostly  
6   evidence in the III and IV and V class and not so  
7   much even well-designed cohort studies or RCTs  
8   that address this either with sham control or some  
9   other form of control.  
10  And I want to just conclude my section  
11  of this before turning it over to Dr. Bian, just  
12  focusing on an issue that I think is a very  
13  relevant clinical question, that being the  
14  development of subsequent fractures after the  
15  procedure. And we have already heard about the  
16  first paper highlighting the relatively low risk,  
17  about 12.4 percent of new symptomatic fractures,  
18  which seems to be at least historically  
19  concordant, or maybe even less than what would be  
20  seen with the natural history of vertebral  
21  compression fractures. A study, though, looking  
22  at kyphoplasty, which was published in the Journal  
23  of Spine, showed a higher risk, a 26 percent risk  
24  of subsequent fractures, with the majority in both  
25  of these studies being fractures at adjacent

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1 levels, and I believe the next speaker will  
2 comment on some of the biomechanical  
3 considerations that might predispose.  
4 So what could these be? Well,  
5 vertebrae treated with polymethyl methacrylate are  
6 stiffer than fractured vertebrae, and in some of  
7 the biomechanical studies that have been done, the  
8 increased stiffness and load was transferred to  
9 the adjacent vertebrae and resulted in unfavorable  
10 biomechanics, and that's been shown also in some  
11 modeling studies where there was an elevated load  
12 to the adjacent levels.  
13 I want to turn the program briefly over  
14 to Dr. John Bian, a health services researcher who  
15 is part of our Centers for Education and Research  
16 on Therapeutics, and John will highlight a study  
17 that is underway and really points out a couple of  
18 things, both where there is a lack of evidence and  
19 also what the methodological challenges are in  
20 doing research in this area. John.  
21 DR. BIAN: Thank you so much. I'm glad  
22 to be here, even though I broke my arm in the car  
23 while coming here. This is an ongoing project;  
24 its aim is to investigate outcomes related to  
25 vertebroplasty. I would like to emphasize, this

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1 is a collaborative effort of UAB, the FDA and our  
2 local Blue Cross Blue Shield of Alabama, and it  
3 has been an honor to be working with them.  
4 Although I am unable to present the  
5 results of our project because our study is still  
6 at the very preliminary stage, but we believe our  
7 project will provide, at least emphasize,  
8 highlight some of the gaps and limitations in  
9 study design used to assess outcome associated  
10 with vertebroplasty.  
11 We have a couple objectives in our  
12 study. The primary objective is to assess risk  
13 for recurrence of vertebral compression fractures  
14 (VCF) for a period up to 24 months following a  
15 vertebroplasty. Secondary objectives include,  
16 one, to determine characteristics of patients  
17 receiving the procedure as well as the providers  
18 who perform the procedure, and to examine the  
19 association of procedural characteristics with  
20 short-term outcomes. Please keep in mind, the  
21 rest of the discussion will be centered around the  
22 primary objective.  
23 Based on our careful literature review,  
24 we have hypothesized that people who have  
25 vertebroplasty are associated with a higher risk

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1 of recurrent fracture. This study will be a  
2 retrospective cohort study which uses a  
3 nonequivalent control group with a pre and post  
4 assessment. It is analysis of administrative data  
5 as well as medical record reviews.  
6 We are going to use two major data  
7 sources. The first is the administrative data on  
8 Blue Cross Blue Shield, which covers approximately  
9 a 3 million population, most of them under the age  
10 of 65. The information we got from them,  
11 including the administrative claims files, which  
12 consists of inpatient-outpatient submitted claims,  
13 as well as pharmacy claims data. We also  
14 retrieved information on patient demographics and  
15 provider specialty. Because of the nature, the  
16 asymptomatic nature of VCF as well as the  
17 sensitivity and specificity, we were not able to  
18 always use the claims data to identify the  
19 procedure, so we also used a targeted medical  
20 review, which included the filings of the claim  
21 for the patients and we also looked at the records  
22 both prior to and at the time of vertebroplasty.  
23 The information we retrieved pertained to spinal  
24 treatment levels, surgical approaches, techniques,  
25 material used, as well as the perioperative

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1 adverse events.  
2 Because the panel has repeatedly asked  
3 questions about control comparison groups, I want  
4 to spend a little more time on this particular  
5 slide. We think it's very important to answer the  
6 question whether the vertebroplasty may lead to a  
7 potential bad outcome. It's very, we define two  
8 groups, we call it exposed group or the treatment  
9 group, and the unexposed group or comparison  
10 group. It's relatively straightforward to define  
11 treatment group, including the VCF patient who  
12 actually underwent vertebroplasty.  
13 The challenge is how to construct a  
14 comparison group. There is no one way to do that,  
15 there are a number of ways to do it, and we spent  
16 a lot of time in putting together a relatively  
17 reasonable appropriate comparison group. So we  
18 have, we're looking for several potential  
19 candidates. One we call a concurrent, which we  
20 focus on VCF patients who did not receive  
21 vertebroplasty during the same time we defined the  
22 treatment group patient. Now there is limitation  
23 because really we do not know, even though we have  
24 observed information on the difference in  
25 characteristics of two groups, but still they are



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1 likely to have some unobserved characteristics  
2 that we would not be able to control. So we  
3 constructed another, a second potential comparison  
4 group which would look at the period before the  
5 window used to define the treatment group patient,  
6 focus on that window, again the patients in that  
7 antecedent group who did not receive a  
8 vertebroplasty.  
9 We also looked at some other  
10 possibilities. For instance, we focused on the  
11 patient who had a severe osteoporotic fracture,  
12 who was in hospitalization, so we can look at  
13 subgroups in each of the two unexposed groups to  
14 see how they compare to the treatment group  
15 patient. I will be glad to answer more questions  
16 on this slide after I finish this talk.  
17 Once we identified a study cohort, we  
18 defined the index event which signaled the  
19 prospective and retrospective follow-up of the  
20 patients. The index event for the treatment group  
21 was the first vertebroplasty, whereas the index  
22 event for the comparison group was the first VCF  
23 diagnosis.  
24 There are a number of variables of  
25 interest. The key variable is outcome variable,

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1 which is the VCF post-index event. There are  
2 other ways to measure outcomes. We can look at  
3 the frequency of recurrent VCF post-index events.  
4 We can also look at the time to a recurrent VCF  
5 post-index event. We could also potentially look  
6 at the rate of frequency on VCF at adjacent  
7 treatment level, so there are a couple options to  
8 look at. The key variable is self-explanatory  
9 compared to treatment versus comparison. There  
10 are other companion covariates which may include  
11 patient demographics, severity of osteoporosis,  
12 comorbidities, provider characteristics such as  
13 specialties, as well as the number of treatment  
14 levels.  
15 Our statistical approach is relatively  
16 straightforward. We used matching to reduce the  
17 number of comparison patients because of the  
18 consideration of (inaudible). Once we determined  
19 who to study, we also used a multivariable case  
20 mix just based on observed characteristics, and I  
21 have discussed that in the previous slides.  
22 Compared to what's in the literature,  
23 our study has a number of advantages. The key  
24 strength using the claims data analysis with the  
25 comparison group is that it can provide timely

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1 information on effectiveness and the safety of  
2 vertebroplasty. And we use a comparison group  
3 which allows to us to control the baseline  
4 differences. Equally important, we focus on --  
5 most other studies focus on pain relief and  
6 improvements in functional status. Our focus is  
7 on the recurrent VCFs, which have been speculated  
8 potentially as an adverse outcome of  
9 vertebroplasty.  
10 Our study has some inherent  
11 limitations. By design, this study is subject to  
12 unobserved confounders. We also have concern  
13 about diagnostic detection bias, in other words,  
14 those patients who receive the vertebroplasty are  
15 more likely to have radiologic fallout because the  
16 nature of VCF, these patients are more likely to  
17 have a higher rate of recurrence of VCF. Our  
18 sample size is also an issue, but we are also  
19 looking at extending our time frame to include  
20 more patients or subjects in our study. The last  
21 one is the generalizability issues, because our  
22 data is from the state of Alabama and most are  
23 under the age of 65, but we are exploring the  
24 possibility of taking our study to a Medicare  
25 screening.

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1 In summary, there is a large body of  
2 published evidence that seemingly supports the  
3 short-term pain relief associated with  
4 vertebroplasty. There is especially a risk of  
5 fracture, particularly at adjacent levels, so  
6 there is a need for controlled studies, RCTs  
7 addressing patient outcome, and good patient  
8 follow-up is the gold standard to more definitely  
9 address the effectiveness and safety questions  
10 associated with vertebroplasty. In conclusion,  
11 there is little consensus on what are the  
12 contraindications for vertebroplasty based on a  
13 very limited number of high quality scientific  
14 studies.

15 DR. MCNEIL: Thank you very much, Dr.  
16 Bian. I think what we'll do at this point is,  
17 since you proposed kind of an experimental  
18 approach for the analysis of this, and we will ask  
19 the panelists if they have any questions of you  
20 with regard to your approach. Yes, Dr. Fessler.

21 DR. RESNICK: Am I correct that there  
22 are no functional outcome measures here and the  
23 results simply represent a cohort with recurrence  
24 outcomes only?

25 DR. BIAN: That's correct.

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1 DR. SAAG: There is no way to measure  
2 functional outcomes in an observational data  
3 study, but you can look at other forms of  
4 morbidity or mortality.  
5 DR. MCNEIL: So you're basically using  
6 administrative data?  
7 DR. SAAG: Well, administrative data  
8 with medical record review. Given the limited  
9 data that is available through a medical record  
10 review, our focus is on the radiographic picture.  
11 DR. MCNEIL: Why don't we start with  
12 Dr. Weinstein, and spend a couple of minutes on  
13 this.  
14 DR. WEINSTEIN: How many questions can  
15 we ask?  
16 DR. MCNEIL: You can ask 1.2.  
17 (Laughter.)  
18 DR. WEINSTEIN: First of all, I was  
19 interested in the Swedish study because, you know,  
20 hip fracture, the mortality rate in the United  
21 States is about 30 percent and theirs were less  
22 than 20 percent, so I was curious about that  
23 population that shows comorbidities in these  
24 studies.  
25 The issue of working with this database

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1 with patients that are less than 65 where most of  
2 the studies have been done for people averaging in  
3 the 70s could be confounding and could lead to a  
4 huge problem. Dr. Bian also shared with us your  
5 concerns about what the covariates and variables  
6 are, and this leaves me with hundreds more  
7 questions than answers.  
8 DR. MCNEIL: Okay. Dr. Jarvik? Why  
9 don't we just run along and --  
10 DR. JARVIK: I pass.  
11 DR. SAAG: Would you like us to address  
12 those questions?  
13 DR. MCNEIL: Quickly, sure. It sounded  
14 like he had 500 of them.  
15 DR. SAAG: I will try to remember them  
16 all, but if I skip a couple, John will remind me.  
17 The data is consistent with what I've seen  
18 reported previously with mortality after hip of  
19 about 20 percent, and I'm not sure where you're  
20 getting the 30 percent.  
21 DR. WEINSTEIN: I think it's about 30  
22 percent in the U.S.  
23 DR. SAAG: So again, I can't comment  
24 more specifically about that study. And I think  
25 you've highlighted some concerns that we have

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1 about the studies and I think John has nicely  
2 illustrated some of the limitations. The purpose  
3 of presenting this was not to even really provide  
4 answers, but more to highlight some of the  
5 questions, and what we tried to do is focus on one  
6 particular area where we think this procedure is  
7 of most concern long-term. We've seen data and  
8 will continue to have discussions today about the  
9 short-term effects of the procedure, both in terms  
10 of pain relief, the effects on height restoration  
11 over maybe the longer term, but the key area that  
12 we feel has really been understudied and the  
13 concern that exists for many of us in the medical  
14 community is how do the results of this procedure  
15 compare with the results of medical management two  
16 years or five years or ten years later, and that's  
17 the point of our study. We recognize that it is a  
18 demonstration study and the purpose of it is to  
19 develop methodologies that we can use with other  
20 larger data sets, recognizing that Blue Cross Blue  
21 Shield, as Dr. Bian suggested, has some limited  
22 generalizability.  
23 DR. WEINSTEIN: But Alabama has a  
24 unique population itself, has a unique setting for  
25 health care and may not be as generalizable as

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1 you're alluding to. And just a simple question,  
2 what about the other results on these people?  
3 DR. SAAG: Well, you're right that  
4 Alabama is a health care system that doesn't have  
5 an electronic medical record, and there might be a  
6 problem with that.  
7 DR. MCNEIL: Maybe one more burning  
8 question.  
9 DR. R.G. FESSLER: The burning question  
10 here is a question of relevance of the questions.  
11 Years ago before becoming a physician, I was an  
12 experimental psychologist, and we were always  
13 under the criticism for spending millions of  
14 dollars of the government's money to prove the  
15 obvious or the irrelevant, and I wonder if we're  
16 not doing the same thing here. As a clinician, I  
17 can tell you that if a patient comes in with eight  
18 out of ten pain and we can get them up in 20  
19 minutes with two out of ten pain, it doesn't  
20 matter if we've got a five percent increased  
21 incidence of recurrent fracture two years down the  
22 road.  
23 DR. MCNEIL: That is one of the value  
24 judgments we will come to at the end of the day.  
25 Mark.



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1 DR. FENDRICK: I appreciate that  
2 medical therapy is in fact moving along, as well  
3 as interventional therapy, but I'd like you to  
4 comment on the need for further elucidation of  
5 what might happen in the patients who are  
6 channeled to vertebroplasty and the high  
7 likelihood that they will get other care  
8 interventions that may look like it's the  
9 vertebroplasty that's doing things but it could be  
10 better medical care, being followed, so on. So,  
11 you mentioned your potential covariates, and I  
12 think a major covariate that is not on your slide  
13 is the fact that people might get taken care of  
14 better given the fact that there's more aggressive  
15 care than because they've gotten the procedure  
16 done already.

17 DR. SAAG: That's a very interesting  
18 point, and if your point is a bias because of the  
19 hypothesis, I'm not sure it would make a  
20 significant difference if indeed one is there, and  
21 indeed the bias could be in the opposite  
22 direction.

23 DR. BIAN: We have some information on  
24 the pharmacy claims, so we know what kind of drugs  
25 they have been on, for how long, and those

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1 probably control some of those biases.

2 DR. FENDRICK: It will control some but  
3 not all.

4 DR. MCNEIL: Okay, why don't we move  
5 on? Thank you very, very much. That's an  
6 interesting approach. And we move on before the  
7 break to Dr. Belkoff from Hopkins.

8 DR. BELKOFF: Thanks for inviting me.

9 In the area of disclosure, I think it's fair to  
10 assume that I've done research for practically  
11 every orthopedic company in the United States that  
12 offers support for research. I have served as a  
13 consultant for various companies on typically a  
14 fee for service, providing information for  
15 disputes, things like that, but I'm not a paid  
16 consultant or on staff for any of these companies.  
17 As I understand it, I have been asked  
18 to just kind of peruse the literature and provide  
19 some information to the panel as to whether it's  
20 worth paying for these procedures, whether  
21 vertebroplasty should be reimbursed or whether  
22 kyphoplasty should be reimbursed. In the process  
23 of preparing for this presentation and for a book  
24 that we're working on, I reviewed 449 articles in  
25 the peer reviewed literature up to last month and

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1 of those there is not one, you've heard,  
2 prospective randomized controlled study with  
3 long-term follow-up, okay?  
4 Of that group of studies, there are  
5 perhaps five that I recommend reading and the rest  
6 of them not. Many of them are my own limitations  
7 because my stuff is basic science and  
8 biomechanics, so I can't talk about long-term  
9 follow-up and pain relief. And it gets  
10 frustrating because vertebroplasty has been around  
11 for over 20 years and it's obviously well overdue  
12 to have a definitive study, prospective,  
13 randomized, et cetera, so it gives you little  
14 option. If I had a disclosure to make about bias  
15 or about conflict of interest, it would be toward  
16 clinical outcome studies, and I would like to see  
17 one.  
18 To open my talk, I want to give some  
19 background on osteoporotic compression fractures,  
20 I know you've been sitting here, and the problem  
21 with being the cleanup guy is that I have to maybe  
22 be repetitive with the previous speakers. When  
23 you look at an osteoporotic compression fracture,  
24 the biomechanics of it, the standard treatment  
25 primary indications are pain relief, and then

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1 address the issue of performing correction.  
2 This is kind of the way I see  
3 vertebroplasty. Where you've got an acute or a  
4 complex fracture, should you seek treatment? If  
5 you seek treatment, should it be conservative or  
6 should you go on to have some sort of  
7 interventional procedure, i.e., vertebroplasty?  
8 If the physician decides to go the route of  
9 vertebroplasty, you go to the next step and get  
10 some sort of kyphosis reduction to perform the  
11 correction, and if so, which method should you  
12 choose?  
13 And what I'll do now, since we don't  
14 have any good literature really to support any of  
15 these decision trees, I will try to move around  
16 the edges and tell you what we do know and what we  
17 think is going on from, and maybe from all the  
18 case studies and so forth that are out there, get  
19 a perspective as to what might be going on.  
20 So here's a normal vertebral body  
21 cross-section from an engineering point of view,  
22 which I am, by the way, I've got a Ph.D. in  
23 mechanical engineering. This here has basically  
24 the structure including the columns, and these  
25 columns bear the load of the axial spine. The

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1 column, the strength of these columns is a  
2 function of the spine, because if you notice, not  
3 only do you have less materials there, the  
4 materials are, the collagen and mineral content  
5 ration has been varied, more brittle, you have  
6 fewer, or more atrophied horizontal cross braces,  
7 which in fact makes these columns longer, and the  
8 buckling strength of a column is inversely  
9 proportional to the square of its length. So as  
10 your columns increase in length by a factor of  
11 two, you decrease the strength by a factor of  
12 four. That's why we have osteoporotic compression  
13 fractures.  
14 Plus the fact that the modeling process  
15 (inaudible) creating concentrations in defective  
16 structures, you end up with vertebral body  
17 compression fractures. That's the kind of  
18 mechanical evidence we're looking at. So what  
19 happens with vertebroplasty, what causes the pain  
20 relief mechanism?  
21 Well, it could be thermal. People  
22 hypothesize a thermal effect. Some of the  
23 materials are actually thermal, so they  
24 hypothesize they give off heat and the heat  
25 actually kills the nerves or cooks the nerves. It

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1 could be that the cement that's used as a  
2 copolymer is cytotoxic, possibly so high in  
3 concentrations that it causes necrosis of the  
4 nerves as well. Or it could be simply a  
5 mechanical process that causes the healing.  
6 We looked at a fair amount (inaudible)  
7 back in '98, did a lot of studies, one of which  
8 was looking at measuring temperatures in vertebral  
9 bodies, and when we looked at the various bodies  
10 of cement and so forth and measured temperatures,  
11 and while it's theoretically possible that the  
12 heat could cause thermal necrosis, the fact of the  
13 matter is that we didn't take into consideration  
14 active heat transport due to blood perfusion and  
15 so forth, and what not. The fact that the  
16 temperatures in the central vertebral body were  
17 high enough to cause necrosis is of probably not  
18 so great significance anyway, because there would  
19 be no blood supply to it. The periphery around  
20 the vortex of the vertebral body, the periostomy  
21 has the majority of the nerves, and the  
22 temperatures were not high enough or were not  
23 likely to be high enough to cause necrosis of  
24 those nerves and give you pain relief.  
25 Similar studies have been done in goat

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1 spines that might support our theories in live  
2 goats. The problem there is they happened to use  
3 smaller volumes of cement than they would use in  
4 humans, so it's kind of hard to make a comparison  
5 due to lack of data.  
6 Cytotoxicity, we looked at the  
7 apoptotic effect of monomer on breast cancer  
8 cells, the apoptotic effect on these cells, MCS-7  
9 cells, was very similar to epithelial cells, and  
10 we decided the literature that looked at this was  
11 not even finished, but the concentrations of  
12 monomer that caused apoptosis were orders of  
13 magnitude higher in time, duration and exposure to  
14 create apoptosis in breast cells than would be  
15 likely to have available in vivo after  
16 vertebroplasty. The highest concentrations we  
17 measured in vivo were basically .12 milligrams per  
18 milliliter, and that was a hip replacement  
19 operation and that only was, the exposure time was  
20 three minutes. And this would be expelled through  
21 the lungs within one circulation, one route of the  
22 circulation system of the blood, whereas to kill  
23 these cells in cell culture, we had to have five  
24 to ten milligrams per milliliter, so an order of  
25 magnitude higher, exposed for an hour to create

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1 apoptosis. So it's very unlikely that the free  
2 monomer will filter around to cause neurotoxicity.  
3 So what is it most likely? It's  
4 probably a simple orthopedic situation of  
5 stabilizing the fracture, internal fixation, and  
6 preventing micromotion or motion of the periosteum  
7 which aggravates the nerves, that's something that  
8 has happened.  
9 Now how much vertebroplasty in general  
10 will restore the strength of the specimen, the  
11 vertebral body, how much of that restoration  
12 occurs kind of depends on the properties of the  
13 cement, how much cement you use, and the condition  
14 of the body, but it will generally happen if you  
15 stabilize the fracture, preventing micromotion.  
16 Once again, if you have your son break his arm or  
17 break his leg or his forearm, and getting a cast  
18 or splint, you're preventing micromotion. You  
19 guys are doing it internally with cement instead  
20 of putting the cast on the outside of the  
21 vertebral body.  
22 Again, how much cement do you need?  
23 We've done some studies on a cadaver specimen,  
24 it's not a whole lot, about 30 percent will  
25 restore stiffness and prevent micromotion, and



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1 that's basically about four to six milliliters of  
2 cement. There are reports in the literature  
3 anecdotally of course, that suggest that a volume  
4 as small as 1.2 milliliters of cement will give  
5 pain relief.  
6 Does the cement respond to spine  
7 mechanics, kinetics, and put you at risk for  
8 future fracture? The data is very inconclusive.  
9 From what we have available from a mechanical  
10 point of view, it's unlikely that just putting  
11 cement in will cause a stress concentration and  
12 put you at risk for future fractures. The bottom  
13 line is these patients are osteoporotic, they are  
14 still osteoporotic after vertebroplasty and they  
15 will continue to be osteoporotic, and they are at  
16 higher risk for vertebral compression fractures,  
17 and that's in my opinion the most likely mechanism  
18 and unless we can show otherwise, that's my story.  
19 If I look at formative correction, we  
20 did some work for Kyphon, and I think there is  
21 probably not much doubt that there is some height  
22 restored. We got about 3 millimeters of height  
23 restoration, which is consistent with Dr.  
24 Lieberman's paper with about 2.9 millimeters, that  
25 may change in his subsequent study, but on average

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1 that was kind of what we got. Whether the height  
2 was restored or not, I think is not the real  
3 issue, but let's talk about some other possible  
4 mechanisms other than height restoration.  
5 Some people reported that simple  
6 traction, bringing back the traction devices of  
7 the middle ages, I saw a cartoon once with that on  
8 it.  
9 Hyperextension, placing pillows under  
10 the patient to put them in hyperextension and try  
11 to get some height restoration or some kyphosis  
12 reduction, there was one report of that.  
13 Vertebroplasty itself was reported as  
14 getting a height restoration on the order of 2.5  
15 millimeters which Hiwatashi reported in some  
16 journals, I'm not sure if it's significant or not,  
17 but it makes for some interesting reading.  
18 And then there's Paul Heini, with a  
19 thing called lordoplasty, where he basically  
20 cemented a medial cannula below the level of the  
21 fracture and then essentially pried the spine back  
22 into alignment and then did a standard  
23 vertebroplasty at the intervening level, and  
24 achieved some height correction or deformity  
25 correction that way. Again, there is one report

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1 in the literature about that.  
2 So, in summary, I wish I had more to  
3 tell you, but the bottom line is we don't even  
4 know what patients are really indicated for  
5 vertebroplasty, what constitutes an acute  
6 compression fracture versus a chronic compression  
7 fracture, how long is acute and how long is  
8 chronic, when do you transfer over. Which  
9 patients respond better to vertebroplasty or  
10 kyphoplasty, and which patients don't? All those  
11 sorts of things haven't been sorted out.  
12 There was that one study that was  
13 nonrandomized, although it was prospective, had a  
14 very limited number of patients and you can  
15 explain yourself. The Australian study that  
16 compared to the conservative group and as you  
17 know, they found that there was a short-term  
18 benefit of pain relief but long-term didn't seem  
19 to make a whole lot of difference. That stands to  
20 reason from my perspective. Again, my opinion is  
21 that once they have stabilized a fracture,  
22 provided internal fixation, allowed a stable  
23 environment for healing to occur and then as the  
24 fracture heals in six to ten weeks, you would not  
25 expect a huge difference in those two patient

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1 groups. Now long-term, there might be a  
2 difference two or three years down the road, I  
3 don't know, because the information is not  
4 available.  
5 If you decide to go to the next step  
6 and look at kyphosis or deformity correction, and  
7 there's a lot of theoretical benefits to this, if  
8 you can show that there is a decrease in premature  
9 sentiety, lung capacity, if there is a decrease in  
10 depression with patients who have a more normally  
11 aligned spine, if there is a decrease in secondary  
12 fractures or fibrosis, then those are all, I  
13 think, very good reasons to consider a kyphosis  
14 reduction procedure. But that has to be shown,  
15 and so far that information is not there.  
16 And then once you decide that that is  
17 important, that creating an anatomically correct  
18 spine or anatomically aligned spine is important,  
19 then you decide which procedure do you want to  
20 pick from, and which of these is better than  
21 others. Is hyperextension with pillows better  
22 than kyphoplasty or lordoplasty, what are the  
23 benefits of all this, and again, the bottom line  
24 is the information is just not there.  
25 So, that's kind of a whirlwind tour of

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1    how I perceive the literature to date.  
2    DR. MCNEIL:  Thank you very much,  
3    Dr. Belkoff.  Is there a question or two for him?  
4    I would like to just ask one question.  You  
5    mentioned that you didn't know when fractures  
6    became chronic?  
7    DR. BELKOFF:  Correct.  I read some  
8    study that divided the patients into two groups,  
9    one fracture is less than a year, one fracture is  
10   more than a year, and I would suggest that a  
11   fracture that is a year old is probably comminuted  
12   and not acute, but I'm not a physician and I think  
13   Dr. Weinstein might better address that question.  
14   DR. MCNEIL:  It might be useful for us  
15   to get a handle on exactly what chronic is,  
16   because we have to make a decision about our  
17   judgments on the basis of acute or subacute,  
18   versus chronic.  
19   DR. PHURROUGH:  We defined it as six  
20   months.  
21   DR. R.G. FESSLER:  For chronic or for  
22   subacute?  
23   DR. MCNEIL:  Chronic.  Any questions  
24   for Dr. Belkoff?  
25   DR. WEINSTEIN:  I think the question

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1 about pain is interesting. We have heard some  
2 presentations talking about deformities, sagittal  
3 alignment, and these may be important, but pain is  
4 important. And you hypothesize that the cement  
5 may have some effect on the pain receptors. I  
6 think there are a lot of patients that get better  
7 and as Dr. Lieberman said, only about a third of  
8 these patients actually show up for treatment. So  
9 why aren't those patients painful, why are you  
10 hypothesizing this?  
11 DR. BELKOFF: I missed the part about  
12 showing up.  
13 DR. WEINSTEIN: There are patients that  
14 have vertebral fractures that don't have  
15 treatment, we know that. Dr. Lieberman suggested,  
16 and I think the Swedish study said there are  
17 fractures of the vertebrae that don't have  
18 mechanical interventions.  
19 DR. BELKOFF: I think there is under  
20 recognition of fractures, I think this is similar  
21 to sacral fractures, where patients may have pain  
22 short term but don't seek attention. They may do  
23 guarding, say I felt something in my back, had  
24 pain for a few weeks, it went away, I didn't want  
25 to seek -- my grandfather was that way, he

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1 wouldn't go to a doctor to save his life and in  
2 fact he didn't, but he would not seek medical  
3 attention. And we saw from the Australian study,  
4 and you probably see a lot of in your own clinic,  
5 those who show up in your clinic who have  
6 compression fractures but have no pain associated  
7 with those fractures?  
8 DR. WEINSTEIN: I usually don't see  
9 someone without pain. Do you have an information  
10 about how it affects the pain in a biomechanical  
11 study?  
12 DR. BELKOFF: I didn't talk about --  
13 when I said that there's certain models where it's  
14 being restored and so forth, these are just the  
15 studies, and there is no way I can measure pain,  
16 but I'm hypothesizing that restoring stability to  
17 the spine is probably a mechanism that causes the  
18 pain relief.  
19 DR. WEINSTEIN: I was trying to make it  
20 clear for the listeners (inaudible).  
21 DR. BELKOFF: It's very hard to do.  
22 That's why I'm so interested to see a clinical  
23 trial, for instance, looking at, documenting the  
24 amount of cement that was injected and seeing if  
25 there's a dose-response relationship, how much

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1 cement do you need? Certainly the less you use,  
2 presumably you decrease the risk for subsequent  
3 injuries with lower applications. But right now,  
4 other than cadavers, and no cadaver needs to have  
5 to restore their strength, so I have no idea what  
6 that would be clinically in terms of pain relief  
7 and long-term outcomes and as you can tell from my  
8 demeanor, I'm a little frustrated with the lack of  
9 clinical information.

10 DR. MCNEIL: I think with that, that  
11 would be a good time to take a break. So, we  
12 actually have a 15-minute break but I would like  
13 to say one thing before the break. We have some  
14 scheduled public comments that start at 10:15 that  
15 go for an hour. We have 15 speakers, that means  
16 four minutes each, and I would like to be  
17 advocates of Doctors Mathis and McKiernan, the  
18 last two speakers. So if the first speakers eat  
19 up their time, they're not going to be happy,  
20 because they won't have any time, so we're really  
21 going to keep the public discussion session  
22 moving. Thank you.

23 (Recess.)

24 DR. MCNEIL: Thank you all for joining  
25 us. I realize I omitted something very important



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1 for our speakers this morning, so I need to ask  
2 Doctors Mark, Lieberman, Saag, Bian, each one of  
3 them individually if they would come to that  
4 microphone and make any statements about conflicts  
5 of interest, and that would include consulting  
6 fees, stocks, stock options, or any other  
7 financial remuneration related to any of the  
8 products that would be under discussion for  
9 today's meeting, and I will obviously ask  
10 prospectively now each of the speakers to do that  
11 as well. So Dr. Mark, do you have any conflicts  
12 you would like to indicate?  
13 DR. MARK: No.  
14 DR. MCNEIL: Dr. Lieberman, are you  
15 here? Okay. Dr. Saag? Not here. Dr. Bian? Not  
16 here. Dr. Belkoff.  
17 DR. BELKOFF: I received research funds  
18 from Stryker, Almedica, Zimmer, DePuy, I don't  
19 know, basically every orthopedic company that does  
20 research have assisted me at one point or another.  
21 Companies that are start-ups. I get royalties for  
22 vertebroplasty work, not from every one that has  
23 been made or sold, but there is still a royalty  
24 agreement with them. There are various company  
25 fee for service, and it's all related to Hopkins,

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1 and I can tell you they are the most draconian  
2 when it comes to conflicts of interest, it clears  
3 their board, if they weren't happy with the  
4 information they had on file, it won't happen. As  
5 far as stocks, I think I have a little bit of  
6 Zimmer stock somewhere.  
7 DR. MCNEIL: Thanks very much. Did Dr.  
8 Saag and Bian come back? We can ask them later  
9 then. With that, what I would like to do to make  
10 this session move along, I would like the next  
11 speaker always to sit in the speaker-ready chair  
12 so we can make sure everybody gets their fully  
13 allocated period of time. So we'll now hear from  
14 Greg Przbylski.  
15 DR. PRZBYLSKI: I know it's a tough  
16 one. I'm Greg Przbylski. I'm a professor of  
17 neurosurgery at Seton Hall University and director  
18 of neurosurgery at the New Jersey Neuroscience  
19 Institute at JFK Medical Center in Edison, New  
20 Jersey. Today I'm speaking on behalf of the North  
21 American Spine Society as board member and  
22 co-chair of the counsel on socioeconomic affairs.  
23 I do not have any stock or formal financial  
24 interest in any orthopedic device company or  
25 receive financial support from any orthopedic

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1 device company other than what may be in my  
2 retirement mutual funds. My transportation today  
3 was paid for by the North American Spine Society.  
4 I have served on advisory committees which  
5 evaluated these devices as well as the  
6 reimbursement committees of the North American  
7 Spine Society as well as the American Association  
8 of Neurological Surgeons and the Congress of  
9 Neurological Surgeons. I have not been contacted  
10 by an orthopedic device company prior to this  
11 meeting to discuss anything that I'm presenting to  
12 you today.  
13 NASS, who I'm speaking on behalf of, is  
14 a multidisciplinary nonprofit educational society  
15 representing physicians who are interested in  
16 spine care. There are more than 4,000 members,  
17 including physiatrists, radiologists, orthopedic  
18 surgeons and neurosurgeons. Clearly from the  
19 presentations this morning, we have heard that  
20 with an aging population, many of whom have  
21 osteoporosis, that development of vertebral body  
22 compression fractures is an important cause of  
23 pain and disability in the Medicare population.  
24 Many of these patients have transient  
25 pain, as has been pointed out, and usually respond

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1 to a period of time and use of opiates or other  
2 medications to resolve their pain. I think an  
3 important thing that has been brought out this  
4 morning that perhaps ought to be clarified is that  
5 nonoperative treatment does help a lot of these  
6 patients, and that the question that Dr. McNeil  
7 asked earlier, what is that denominator, what is  
8 the total population that we're looking at, versus  
9 the population that is going to be treated?  
10 Speaking on behalf of myself and my  
11 colleagues at our institution, I would estimate  
12 that fewer than ten percent of patients with  
13 vertebral body compression fractures actually  
14 undergo a subsequent treatment such as  
15 vertebroplasty or kyphoplasty. It is that small  
16 subset that really is not addressed in the Diamond  
17 study that has already been presented. That was a  
18 small study that really looked at a six-week time  
19 limit for post-treatment compared to a  
20 nonoperative treatment, and I would submit that  
21 many of those patients are getting better in that  
22 first six weeks. In our personal practice, we are  
23 typically not treating those patients until they  
24 have gotten into that subacute phase which I would  
25 estimate as being somewhere six weeks after they

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1 sustain the fracture, and if they continue to be  
2 symptomatic at that point, that's when we treat  
3 them.  
4 For these patients, the North American  
5 Spine Society believes that both vertebroplasty  
6 and kyphoplasty offer early rapid post-operative  
7 pain relief and allow restoration of function, and  
8 reduction or elimination of the use of opiate  
9 medications or other medications for managing  
10 their pain. The results of both treatments we  
11 believe are similar and that although the data  
12 does suggest, as has been pointed out this  
13 morning, a smaller leak rate by kyphoplasty, the  
14 data does not support the fact that that is  
15 clinically relevant. As we've seen, the outcomes  
16 of morbidity and mortality are similar between the  
17 two procedures. Both treatments may in some  
18 patients restore in part vertebral body height and  
19 reduce angulation.  
20 It is also estimated that the physician  
21 work with both procedures is similar and has  
22 recently been reviewed by relative value update  
23 committee, of which I represent the AA and NASS  
24 at, and the conclusions of the multidisciplinary  
25 relative value update committee was that the

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1 physician work was similar between the two  
2 procedures.  
3 The North American Spine Society  
4 requested a tracking code for the procedure of  
5 kyphoplasty, recognizing the fact that the  
6 literature, as we've heard this morning, is  
7 somewhat incomplete. We requested a tracking code  
8 to give additional time for additional literature  
9 to be developed, for additional comparisons to be  
10 played, to really determine whether there is a  
11 difference between kyphoplasty and vertebroplasty.  
12 Naturally, since both procedures are  
13 equally effective in the treatment of subacute  
14 vertebral body compression fractures that persist  
15 despite the duration of nonoperative treatment, we  
16 would support a coverage decision for both  
17 procedures in the subacute patient and recommend  
18 that facility and non-facility payments for both  
19 those procedures are based on the least expensive  
20 supply costs and that the determination of  
21 hospitalization is really based on not the  
22 procedure but the comorbidities of the patient to  
23 justify hospitalization.  
24 I would like to thank the members of  
25 the MCAC for the opportunity to discuss both of

00103

1 these procedures and share the viewpoints of the  
2 North American Spine Society about vertebroplasty  
3 and kyphoplasty.

4 DR. MCNEIL: Thank you very much.

5 Dr. Jensen.

6 DR. JENSEN: My name is Lee Jensen. I  
7 am the director of interventional radiology at the  
8 University of Virginia and have experience with  
9 vertebroplasty. I am speaking on behalf of  
10 several radiologic societies. I do not own any  
11 stock related to these devices. My transportation  
12 was paid for by the ASITN. I am currently not on  
13 any paying boards. I have been a (inaudible) for  
14 Carolax over a year ago, and have also been a  
15 consultant to the FDA orthopedics panel in the  
16 past.

17 On behalf of the combined membership of  
18 the American Society of Interventional and  
19 Therapeutic Radiology, the Society of  
20 Interventional Radiology and the Society of  
21 Interventional Radiology, I would like to thank  
22 the board for allowing us to comment on this  
23 exciting topic. It is the position of the society  
24 that vertebroplasty is a safe, efficacious and  
25 durable procedure in appropriate patients with

00104

1 systematic osteoporotic and neoplastic fractures  
2 that have failed medical therapy. This procedure  
3 is offered only when traditional medical therapy  
4 has not provided pain relief or pain is  
5 significantly altering the patient's life style.  
6 Since 1987, multiple case series and  
7 retrospective and prospective nonrandomized  
8 studies have shown statistically significant  
9 improvement in pain and physical activity, with  
10 response rates usually in the 80 to 95 percent  
11 range. These results have been confirmed in two  
12 prospective studies when compared to a control  
13 group, and a prospective randomized controlled  
14 study. In the Diamond study of 79 patients, 55  
15 patients treated with vertebroplasty showed  
16 statistically significant improvement in pain and  
17 mobility compared to the nonrandomized control  
18 group of 24 patients.  
19 Please keep in mind that all the  
20 vertebroplasty patients had an MR documentation of  
21 acute pressure fractures, but only 65 percent of  
22 the self-selected controls agreed to MR, making  
23 the etiology of pain unclear in 35 percent of this  
24 group. In this study 42 patients were  
25 hospitalized for pain control; those treated with



00105

1 conservative therapy remained in the hospital on  
2 average six days, or 40 percent longer than the  
3 vertebroplasty group.  
4 In a study published this year from  
5 Kodiyashi, et al., of 175 patients, 96.4 percent  
6 showed statistically significant improvement in  
7 pain at 24 hours after vertebroplasty, a pattern  
8 of pain relief not seen in natural history. The  
9 pain relief was complete in 44 patients. 94 of  
10 115 immobilized patients, or 81.7 percent, were  
11 mobile by 24 hours after vertebroplasty.  
12 Retrospective comparisons with a control group of  
13 80 patients treated conservatively showed the  
14 average time of ambulation in that group was 24  
15 days, over three weeks longer than the  
16 vertebroplasty group. In fact, seven patients  
17 never became ambulatory.  
18 In a prospective randomized controlled  
19 trial done by Jobe, et al., 40 patients were  
20 randomized to vertebroplasty versus conservative  
21 therapy. All vertebroplasty patients showed  
22 statistically significant improvement in pain and  
23 activity levels and decreased medication use. The  
24 medical therapy group showed no change in these  
25 parameters at six weeks. 16 of the 19 patients

00106

1 were allowed to swap after six weeks. After  
2 receiving the vertebroplasty, they too showed  
3 statistically significant improvement in pain and  
4 mobility. Overall outcomes at one year using the  
5 SF-36 showed that both treated groups showed  
6 significant improvement in most of the subscales,  
7 demonstrating the durability of the procedure.  
8 The benefits of vertebroplasty far  
9 outweigh its risks when compared to conservative  
10 therapy and its success rate is consistently high,  
11 thus remaining cost effective and producing  
12 immediate improvement in patients' quality of  
13 life, primarily through the alleviation of pain  
14 and rapid return to ambulation, in addition to  
15 reducing the need for skilled care, expensive  
16 drugs or orthopedic devices which have not  
17 undergone randomized controlled prospective  
18 trials. A return to ambulation can reduce other  
19 adverse outcomes, including mortality in elderly  
20 patients confined to bed. Vertebroplasty is an  
21 effective and appropriate therapy for the  
22 treatment of vertebral compression fractures, and  
23 it is the recommendation of the societies that  
24 vertebroplasty be a covered service for the  
25 medical indications outlined in the published

00107

1 data. Thank you for your attention.  
2 DR. MCNEIL: Dr. Hirsch. Thank you.  
3 DR. HIRSCH: Thank you. My name is  
4 Josh Hirsch, and I am an interventional  
5 radiologist at Massachusetts General Hospital,  
6 speaking on behalf of the ASITN, who funded my  
7 travel. As I was unaware that I would be  
8 addressing this auspicious committee today, I have  
9 not previously presented the following disclosure,  
10 and I apologize for not having provided it. I am  
11 a physician advisor to ArthroCare, Cardinal  
12 Health, and others in orthopedic technology, and  
13 in the past I have received honorarium checks for  
14 presentations.  
15 Choosing a topic to present in four  
16 minutes is indeed a challenge. As was previously  
17 mentioned by Dr. Lieberman, I would like to  
18 emphasize that I do believe we are talking about  
19 tools in a toolbox. Our practice is (inaudible)  
20 unhappily or happily seeing less so than before,  
21 and that we routinely perform vertebroplasty and  
22 kyphoplasty, and do large volumes of both of these  
23 procedures.  
24 Speaking colloquially, if we just  
25 review the extensive literature, we will forget

00108

1 the human aspect of this procedure, and it's my  
2 opinion that we cannot forget this human aspect.  
3 The remarkable impact that this has had on  
4 patients' lives has forced a change in my practice  
5 and the fact that I spend a great deal of my time  
6 doing these procedures.  
7 I think there are a couple groups in  
8 society that demonstrate the success of this. A,  
9 patients who have had a fracture before, in my  
10 experience, almost never want to go to  
11 conservative therapy, they want to be treated  
12 almost immediately. Also, physicians that have  
13 been cited in papers that are experts in medical  
14 management routinely refer their patients to my  
15 practice for treatment with both vertebroplasty  
16 and kyphoplasty.  
17 In the pursuit of science, it takes  
18 dedication to (inaudible) and Dr. Kallmes of  
19 course is the principal investigator of that  
20 trial, and both Dr. Kallmes and Dr. Jarvik  
21 (inaudible) this to be done. They cited as  
22 reasons the extensive literature supporting  
23 vertebroplasty and decided to proceed with  
24 vertebroplasty only, and the considerations of a  
25 sham trial. I think it should be pointed out that

00109

1 I was willing to challenge my own ethics to  
2 participate in a sham trial because of the  
3 crossover possibility. I believe there is  
4 extensive data to demonstrate that treating  
5 conservatively in patients that are bedridden,  
6 et cetera, is the same as no treatment at all.  
7 I myself have cited David Kallmes'  
8 abstract for the sham trial feasibility, and I  
9 think that it was never the purpose of that  
10 abstract to serve as a pivot point in discussions  
11 regarding the validity of vertebroplasty as a  
12 procedure, rather the inability to do the sham  
13 trial. I would point out that I think in Boston,  
14 it has become near the standard of care to perform  
15 one of these treatments for a compression fracture  
16 and I think it would be extremely difficult to  
17 actually randomize patients into this type of  
18 trial, and I think this reflects a national  
19 experience.  
20 I guess in closing what I would like to  
21 do is invite members of the committee, there are  
22 many speakers here today, the human aspect of the  
23 story is real, to discuss the clinical impact on  
24 patients without thinking about that is really not  
25 right, and I invite you to come to my clinic or

00110

1 any of the physicians' clinics that are here and  
2 see whether or not the implied cohort is a real  
3 phenomenon. I thank you.  
4 DR. MCNEIL: Thank you very much,  
5 Dr. Hirsch. Dr. McGraw.  
6 DR. MCGRAW: I'm Dr. Kevin McGraw, an  
7 interventional radiologist in Columbus, Ohio. I  
8 need to disclose that I am a physician advisor for  
9 Cardinal Health and also ArthroCare Spine. I am  
10 representing today the Society of Interventional  
11 Radiology, who paid for my travel. I want to  
12 thank you very much for this opportunity to speak  
13 to you today about this very important topic.  
14 When considering treatment options for  
15 compression fractures, you must ask yourself and  
16 tell yourself that conservative therapy is not  
17 without risks. Patients are often placed on  
18 conservative therapy which includes bed rest,  
19 immobilization, or narcotic analgesics. During  
20 bed rest, virtually every organ is adversely  
21 affected, and that is going to be more pronounced  
22 in elderly patients. Bone density declines about  
23 two percent per week in patients who already  
24 suffer from osteoporosis, muscle strength declines  
25 about one to three percent per day or 10 to 15

00111

1 percent per week. Nearly half of all strength is  
2 lost within the first three to four weeks of bed  
3 rest. Other complexes are also affected by  
4 immobilization, leading to contractions, which are  
5 more prone to develop in elderly patients.  
6 There's a lot of evidence to show that early  
7 immobilization after initial stabilization can  
8 lead to contracture formation.  
9 Early mobilization also decreases the  
10 amount of pressure sores that can develop. There  
11 were studies done of pressure sore development in  
12 patients 70 years or older. Once a pressure sore  
13 or decubitus ulcer does develop, nursing calls  
14 increase by as much as 50 percent with a total  
15 treatment of one pressure sore being estimated to  
16 be 15,000 to \$20,000.  
17 In patients placed on bed rest, they  
18 have a risk of developing deep venous thrombosis  
19 61 percent of the time. Pulmonary embolism can be  
20 sustained in up to 10 percent of the patients with  
21 fatal PE seen in 0.5 to 10 percent of patients.  
22 If we subject a patient to six weeks of  
23 bed rest, they've lost 12 percent of their bone  
24 density, half of their muscle strength, they  
25 develop a decubitus ulcer, and they have a 10

00112

1 percent chance of a PE. In a recent study by  
2 Brown, et al., in which almost 500 patients with  
3 compression fractures were followed, they received  
4 conservative therapy only, they were divided into  
5 three groups, low mobility, intermediate mobility  
6 and high mobility. It was found that patients  
7 with low and intermediate mobility, that these  
8 were independent predictors of poor outcomes at  
9 discharge, with poor outcomes being defined as a  
10 decline in activities of daily living, repeat  
11 hospitalization or death.  
12 Since vertebroplasty results in early  
13 mobilization, the SIR, ASITN and ASNR believes  
14 that vertebroplasty is superior to conservative  
15 treatment. To summarize, vertebroplasty increases  
16 mobility, increased mobility decreases patient  
17 morbidity and mortalities. Thank you very much.  
18 DR. MCNEIL: Thank you. Dr. Richard D.  
19 Fessler.  
20 DR. R.D. FESSLER: Good morning. I am  
21 Richard D. Fessler, I am an associate professor of  
22 neurosurgery, radiology and neurology at Wayne  
23 State University School of Medicine in Detroit. I  
24 am speaking on behalf of the American Association  
25 of Neurological Surgeons and the Congress of



00113

1 Neurological Surgeons, who funded my travel here  
2 today. I do not have any financial disclosures to  
3 make with regard to any orthopedic company.  
4 On behalf of the American Association  
5 of Neurological Surgeons and the Congress of  
6 Neurological Surgeons, I would like to thank you  
7 for allowing me to be here today to present our  
8 views regarding the use of vertebroplasty and  
9 kyphoplasty for the treatment of vertebral body  
10 compression fractures. The AANS and CNS consider  
11 vertebroplasty and kyphoplasty to be safe,  
12 effective and durable treatments for relief of  
13 pain due to osteoporotic or malignant compression  
14 fractures. When performed in accordance with  
15 published protocols, those procedures offer  
16 immediate pain relief for those patients who are  
17 not improving on conservative treatment.  
18 Vertebroplasty and kyphoplasty should be available  
19 to Medicare patients when deemed appropriate by  
20 their treating physicians.  
21 When a patient does not improve within  
22 several weeks, we do not believe that the patient  
23 should be required to endure the pain and  
24 disability of an additional waiting period when we  
25 have procedures that can alleviate such suffering.

00114

1 For these patients, acute pain relief, acute  
2 quality of life and mobility should not be  
3 withheld by the benefit of vertebroplasty or  
4 kyphoplasty when indicated.  
5 Conservative treatment itself has been  
6 shown to pose significant risks. In the elderly  
7 population, immobilization, prolonged bed rest and  
8 narcotic pain medication has serious health  
9 consequences. The risks and benefits of  
10 vertebroplasty and kyphoplasty have been  
11 thoroughly examined over the last several years,  
12 and if these procedures are not available, other  
13 medical and surgical alternatives may have greater  
14 complications, especially in the elderly  
15 population. We believe that vertebroplasty and  
16 kyphoplasty should be reimbursed appropriately.  
17 Again, thank you for the opportunity to  
18 be here today. We have submitted our full  
19 opinions to the evaluative questions that the  
20 panel will be asking. These questions were  
21 carefully considered by a group of experts from  
22 the AANS and CNS joint section on spine and  
23 peripheral nerves, and reflect the clinical  
24 experience that we submit for your consideration.  
25 Thank you again.

00115

1 DR. MCNEIL: Thank you, Dr. Fessler.  
2 Dr. Gold.  
3 DR. GOLD: I'm Deborah Gold, an  
4 associate professor of medical sociology at the  
5 department of psychology and psychology at Duke.  
6 I also serve on the board of directors for the  
7 National Osteoporosis Foundation and chair their  
8 education committee. For disclosures, I have a  
9 consulting relationship with Kyphon, who paid for  
10 my travel today.  
11 I hope I'm speaking for all of the  
12 people who suffer from vertebral compression  
13 fractures in my talk today. It concerns me some  
14 that there is a misconception in this room that  
15 vertebral compression fractures automatically get  
16 better with a nonoperative treatment. That is not  
17 at all what the data show. After a vertebral  
18 compression fracture, patients show no significant  
19 improvement at six months in pain, function or  
20 disability. Two years after a fracture, patients  
21 still show no improvement in physical function,  
22 and they remain physically impaired five years  
23 after their last vertebral compression fracture.  
24 These last two studies used the SF-36 as their  
25 point of departure.

00116

1 Nonoperative care doesn't always  
2 prevent spinal deformity. We know that people who  
3 have a fracture are more likely to have a second  
4 fracture. In a study of over 200 patients, over  
5 50 percent had fractures that were evident from  
6 the beginning and did not improve. 42 percent had  
7 fractures with continued wedging over six to 18  
8 months, and worsening pain. Patients lost height  
9 in clinical trials for pharmaceutical agents, even  
10 when they were on those drug treatments.  
11 To me, the most important thing for you  
12 to understand today is that the impact of  
13 vertebral compression fractures goes beyond the  
14 spine. When the body configuration changes, the  
15 pulmonary function is limited because the thoracic  
16 area is restricted. Too, the abdominal area is  
17 restricted and there is gastric distress,  
18 including loss of appetite due to that abdominal  
19 restriction. All kinds of compensatory mechanisms  
20 reduce gait velocity, affect balance, and create  
21 chronic fatigue. And despite the fact that many  
22 physicians have dismissed vertebral compression  
23 fractures as not worth paying attention to, there  
24 is increased mortality with these fractures, due  
25 to both fracture severity and hyperkyphosis.

00117

1 And here are the people I'm talking for  
2 and telling you that these people did not have  
3 access to operative care, and you can see that  
4 fracture begat fracture, and the physical  
5 consequences are obvious.  
6 Here we see that vertebral compression  
7 fractures deform, debilitate and disable this  
8 woman in nine years, when she went from being a  
9 person capable of independent ambulation and then  
10 was condemned to a walker.  
11 We also know that in comparison, many  
12 people consider the hip fracture worse than  
13 vertebral compression fractures and yet when we  
14 look at the evidence, we see that the vertebral  
15 compression fracture, patients have lower SF-36  
16 scores in several studies, and have excess  
17 mortality after vertebral fractures greater than  
18 after hip fractures. Here is a visual way of  
19 looking at that, age-matched control, hip fracture  
20 and spine fracture patients. The relative risk of  
21 death in 3.8 years is eight times that of the  
22 age-matched control in the vertebral compression  
23 fracture group.  
24 The impact of vertebral deformity on  
25 quality of life is substantial, and if you look at

00118

1 the quality of life as measured by the SF-36, the  
2 radiographic vertebral fractures, it was  
3 comparable to that of patients with COPD or  
4 cardiac disease. Patients with three or more  
5 radiographic fractures lost of quality of life  
6 comparable to patients with stroke or with cancer.  
7 Thank you very much.  
8 DR. MCNEIL: Thank you very much,  
9 Dr. Gold. Dr. Cher.  
10 DR. CHER: Good morning. My name is  
11 Daniel Cher. My financial interest is that I'm a  
12 Kyphon employee. I'm also a board certified  
13 internist who trained at Yale and Stanford  
14 Universities. I have ten years' experience in  
15 clinical research and seven years' experience in  
16 medical devices.  
17 In the next few minutes you're going to  
18 hear about over two dozen studies on kyphoplasty.  
19 I would like to address two of these studies that  
20 have been referred to, these are concurrently  
21 controlled studies.  
22 The first study involved 36 patients  
23 with osteoporosis who had a single acute fracture.  
24 The mean fracture age was 34 days, and again, this  
25 study enrolled patients in whom there was, quote,

00119

1 functional instability of the vertebral body on  
2 functional study radiographs. Of patients who  
3 chose treatment, that is, they chose either  
4 balloon kyphoplasty or nonsurgical treatment, and  
5 at baseline the groups were very well matched.  
6 Most of the patients were women, mean age was in  
7 the eighth decade, height, weight and concomitant  
8 illness were very well matched.  
9 In subjects treated with balloon  
10 kyphoplasty, pain as measured on a zero to ten  
11 point scale decreased from a mean of 5.4 to 2.0 at  
12 follow-up, a 63 percent decrease. In contrast,  
13 the nonsurgical group had hardly any pain  
14 reduction at all.  
15 Similarly, back function as measured by  
16 the Oswestry Disability Index showed a very large  
17 60-point decrease, and remember that the FDA's  
18 criteria for significant decrease is just 15  
19 points. In contrast, the nonsurgical group had  
20 hardly any change at all.  
21 In the balloon kyphoplasty group no  
22 patients, no patient had worsening of the index  
23 fracture, whereas nearly every patient in the  
24 nonsurgical group had progressive worsening of the  
25 index fracture.

00120

1 37 percent of subjects treated with  
2 balloon kyphoplasty experienced a new fracture in  
3 the six months on follow-up, compared to 65  
4 percent of patients in the nonsurgical management  
5 group.  
6 The second study enrolled 60 patients  
7 with osteoporosis. All subjects had chronic  
8 fractures, and by chronic I mean fractures aged  
9 greater than one year. 40 subjects underwent  
10 balloon kyphoplasty and 20 underwent nonsurgical  
11 management. As in the previous study, the  
12 patients were very well matched at baseline,  
13 including for sex, age, bone marrow density,  
14 number of prevalent fractures and concomitant  
15 illnesses.  
16 On a 100-point pain scale, subjects  
17 receiving kyphoplasty had an 18-point increase,  
18 whereas those treated with nonsurgical management  
19 had hardly an increase. Activities of daily  
20 living were improved. Height, patients treated  
21 with balloon kyphoplasty had a 12 percent increase  
22 in vertebral body height whereas those treated  
23 with nonsurgical management had an 8.2 percent  
24 loss. In the balloon kyphoplasty group 12.5  
25 percent experienced a new fracture and 30 percent



00121

1 of the patients with nonsurgical management  
2 experienced a new fracture.  
3 Putting this study together with the  
4 previous study shows a statistically significant  
5 decrease in the rate of new fractures in patients  
6 treated with balloon kyphoplasty when compared to  
7 nonsurgical management.  
8 And not shown on this slide, there was  
9 also a statistically significant reduction in back  
10 pain visits to physicians over follow-up from nine  
11 visits on average in the nonsurgical group to  
12 three visits on average in the surgical group.  
13 In summary, these two studies provide  
14 strong evidence to support the effectiveness of  
15 balloon kyphoplasty versus nonsurgical management,  
16 and help to answer question number one that the  
17 panel has to consider with respect to the quality  
18 of the evidence. The gain in functional outcomes  
19 of these two studies are consistent with the  
20 entirety of the literature on kyphoplasty. In  
21 addition, they provide strong evidence suggesting  
22 that in comparison to nonsurgical management,  
23 kyphoplasty may reduce the rate of subsequent  
24 fractures. Thank you.  
25 DR. MCNEIL: Thank you very much.

00122

1 Dr. Garfin.  
2 DR. GARFIN: Hello. I am Steve Garfin,  
3 professor and chairman of the department of  
4 orthopedic surgery at the University of  
5 California, San Diego. I specialize in spine  
6 surgery. I am here speaking for kyphoplasty  
7 patients who have obtained benefit from this  
8 procedure. My expenses are being covered by  
9 Kyphon, for which I am a consultant. I and/or my  
10 department have received financial support from  
11 Kyphon, but also from the NIH, VA, and many  
12 companies, some related to today's topic. I am  
13 past president of the North American Spine Society  
14 and the Cervical Spine Research Society. I  
15 coordinated the American Academy of Orthopedic  
16 Surgeons spine educational courses for many years.  
17 I am a deputy editor for Spine. I review articles  
18 for many orthopedic and spine care-related  
19 journals. I have previously been invited to  
20 participate on FDA panels for orthopedic devices  
21 including kyphoplasty. I have participated in and  
22 have co-authored papers on innumerable spine  
23 clinical trials. I was the first person separate  
24 from the inventor to do this procedure, which I  
25 have performed regularly with excellent results

00123

1 since 1999.  
2 Today I'm going to be presenting some  
3 information on a two-year multicenter prospective  
4 study looking at clinical outcomes following  
5 kyphoplasty. 19 centers were involved, 16  
6 community, three university, all had an IRB  
7 approval, all patients signed informed consents.  
8 There were over 200 painful thoracic or lumbar  
9 fractures treated, 155 patients entered into the  
10 study. As one would expect, most were female and  
11 in the obvious Medicare range with an average age  
12 of 77. Fracture age, almost half or more had over  
13 two months of pain, all had failed nonoperative  
14 care. 100 patients were followed for two years.  
15 None of the patients had disabling back pain  
16 secondary to other conditions.  
17 The pain scores were very high  
18 preoperatively and fell dramatically immediately  
19 after kyphoplasty. Activities that we asked the  
20 patient to record were days at bed rest for a  
21 month and mean days of activity interfered with by  
22 pain. Rapidly following kyphoplasty, there was a  
23 significant return to their activity.  
24 We measured activities of daily living,  
25 and three points to look at here are bending,

00124

1 lifting and standing for an hour. Pretreatment,  
2 the patients had marked limitations in function  
3 and inability to perform functions. Immediately  
4 following treatment or at least when they were  
5 able to be recorded and tested, they had dramatic  
6 improvement in their ability to lift, bend and  
7 stand. We used SF-36 outcome data, we looked at  
8 physical domain and mental health domain. There  
9 was a dramatic improvement from pre to post  
10 treatment, 20 to 40 points is markedly  
11 statistically significant. Of importance to me,  
12 the one factor that didn't rise was the general  
13 health. We would not expect our heart, kidneys or  
14 other areas to improve, which adds, to me,  
15 validity to the entire study.  
16 In summary, these patients were highly  
17 debilitated pre-treatment, much more than I  
18 anticipated from the literature or until the data  
19 was seen. There was to me a very compelling,  
20 convincing, rapid, marked, sustained improvement  
21 after undergoing kyphoplasty that lasted the two  
22 years of the study and there were no  
23 procedure-related adverse events. It is clearly  
24 relevant to Medicare and this aged population and  
25 throughout the community. This study, when

00125

1 combined with all the available literature and  
2 scientific presentations that I have read and  
3 heard over the years, has convinced me that  
4 kyphoplasty is the appropriate and perhaps the  
5 conservative care option for many of these  
6 debilitated elderly individuals to get them and  
7 their families a healthier and happier quality of  
8 life.  
9 Thank you for the opportunity to  
10 present my data and to participate in this new and  
11 unique format. If there are any questions that I  
12 as someone who has performed these procedures can  
13 address now or later, I will be glad to try.  
14 DR. MCNEIL: Thank you very much, Dr.  
15 Garfin. Dr. Jolivette.  
16 DR. JOLIVETTE: Good morning. My name  
17 is Dan Jolivette. I am the medical director at  
18 Kyphon and a board certified pediatrician. I have  
19 35 years of clinical research experience,  
20 including ten years as investigator and 20 years  
21 as a researcher in industry. I am currently the  
22 medical director at Kyphon.  
23 I'm here to discuss with you the  
24 balloon kyphoplasty literature and to respond to  
25 all five questions. There are approximately 120

00126

1 articles in the English literature easily  
2 identified on MEDLINE using the search term  
3 kyphoplasty. 28 of these report clinical outcomes  
4 for at least ten patients. As a group, these  
5 studies include over 1,500 patients treated for  
6 pathologic vertebral body fractures due to  
7 osteoporosis or related to cancer. In addition to  
8 the concurrently controlled studies described by  
9 Dr. Cher earlier, there are 14 prospective and 12  
10 retrospective studies. These studies measure a  
11 wide range of clinical inputs including pain,  
12 ambulation, three different validated stability  
13 measuring tools and the widely used SF-36 quality  
14 of life questionnaire in addition to height  
15 restoration and angular deformity. Positive  
16 outcomes were demonstrated following kyphoplasty  
17 in each of these outcome measures in virtually all  
18 studies in which they were measured.  
19 Turning to safety, as part of our 510K  
20 submission for kyphoplasty, the FDA requested a  
21 safety comparison between balloon kyphoplasty and  
22 vertebroplasty. This analysis was last updated in  
23 July of 2004. When we performed a MEDLINE search  
24 for all English language articles on the terms  
25 kyphoplasty and vertebroplasty, we found 77

00127

1 kyphoplasty articles and 363 vertebroplasty  
2 articles. We limited the analysis to only  
3 original articles including results for more than  
4 ten patients and where there was a clear  
5 indication of whether the complication was  
6 procedural or not. The resulting analysis  
7 included 18 studies of balloon kyphoplasty and 39  
8 for vertebroplasty.  
9 The overall procedure-related  
10 complication rate included both bone cement-  
11 related and non-bone cement-related complications.  
12 For kyphoplasty, the rate was 0.9 percent among  
13 897 patients and for vertebroplasty it was 5.44  
14 percent among 2,400 patients treated. This is a  
15 statistically significant difference between these  
16 two groups.  
17 In summary, the clinical outcomes of  
18 over 1,500 patients followed after kyphoplasty are  
19 documented in 28 settings. The positive clinical  
20 effects and outcomes demonstrated in the two  
21 concurrently controlled studies were marked and  
22 underscored the results in the 26 separate case  
23 series that have also been done. In each study  
24 the safety profile of balloon kyphoplasty was  
25 excellent. These studies provide a body of data

00128

1 warranting a positive response to each of the five  
2 questions with a high level of confidence. Thank  
3 you.

4 DR. MCNEIL: Thank you. Dr. Dohm.

5 DR. DOHM: Thank you, members of this  
6 committee, for allowing me to speak to you about  
7 the evidence and the effectiveness of kyphoplasty.  
8 I'm Michael Dohm, a practicing orthopedic surgeon  
9 in western Colorado, and I come before you to  
10 present a clinical application of the evidence and  
11 practice. I am not a paid consultant for Kyphon.  
12 I did have them cover my travel as I was diverted  
13 from San Diego today where a minimally invasive  
14 spine meeting was taking place, but I think it's  
15 important to be here.

16 As a member of the evidence-based  
17 practice committee for the American Academy of  
18 Orthopedic Surgeons, in 1996 I attended our first  
19 national meeting regarding outcomes in Cambridge,  
20 and I heard a presentation which I've made part of  
21 my practice. The presenter spoke about outcomes  
22 focusing, evaluating patient outcomes in terms of  
23 patient satisfaction, function, technique or  
24 technical aspects of the care, and costs. The  
25 speaker was Dr. James Weinstein, who is present



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1 here today. I have been involved in following  
2 patient outcomes in my practice since that time.  
3 Through the Western Slope Study Group,  
4 a quality improvement organization we developed  
5 following Dr. Robert Keller's Maine Medical  
6 Assessment Foundation, I currently follow up on a  
7 number of IRB-approved studies. I present the  
8 following outcomes because I am confident in their  
9 validity and in the process of their evaluation.  
10 There is substantial evidence in the  
11 literature regarding vertebroplasty and  
12 kyphoplasty, as you have heard today. This study  
13 of patients with pathologic fractures, about 264  
14 levels, is representative of what I have seen in  
15 my own practice. 52 patients were evaluated with  
16 pain visual analog scale and Oswestry.  
17 Preoperative and postoperative measures show  
18 statistically significant improvement in scores.  
19 This reflects the results I have seen in my own  
20 office with kyphoplasty.  
21 Patients were also evaluated in terms  
22 of physical, social and emotional function  
23 utilizing the SF-36, as you have heard described  
24 today by Dr. Mark, Dr. Lieberman and others.  
25 These findings, again, show significant changes in

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1 patients undergoing kyphoplasty in terms of  
2 preoperative and postoperative findings. The  
3 challenge, then, is to refute this data or to  
4 produce a better study when discussing outcomes.  
5 If the fracture is an active lesion,  
6 one which has cellular activity and response to  
7 apoptotic change, then these patients benefit from  
8 this surgical intervention, I am confident that  
9 these studies show a net health benefit for these  
10 patients. This study has evaluated the results of  
11 56 candidate patients with multiple myeloma and  
12 metastatic tumors. 22 patients had kyphoplasty  
13 without complications. There was pain relief in  
14 84 percent of them within 24 hours, a significant  
15 decrease in pain medication utilization one month  
16 post-op, and no mortality. We have a cancer  
17 center in Grand Junction, and this again reflects  
18 what I see in my practice.  
19 I perform ten to 14 surgical procedures  
20 a week, which include kyphoplasty and which  
21 represents fewer than ten percent of the patients  
22 that I evaluate and treat weekly. I have a  
23 general orthopedic practice and have been in the  
24 same place for 14 years. I have about 120 patient  
25 encounters a week. I treat patients

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1 conservatively, I manage their osteoporosis  
2 primarily, and I intervene when necessary. I  
3 believe I represent practicing physicians. I  
4 follow both operative and nonoperative patients,  
5 and I have performed kyphoplasty since 2001. I  
6 know the literature and am acutely aware of the  
7 evidence. I believe there is substantial evidence  
8 to support the utilization of kyphoplasty and have  
9 included this in my algorithm for treating  
10 vertebral compression fractures.  
11 I am also a member of the Western  
12 Orthopedic Association, a board member. At a  
13 meeting in San Antonio three years ago, a 73-year-  
14 old orthopedist was recognized for never missing a  
15 meeting in 45 years. In his address he stated  
16 there were four significant advances in orthopedic  
17 surgery, anterior cervical fusion, total hip and  
18 knee replacement, and kyphoplasty. I concur.  
19 Nothing is more heart warming than hearing my  
20 patients' families, thank you for giving us back  
21 our mother, which is truly in reality my patients.  
22 Please help our patients and help to promote and  
23 advance best practice. I believe the evidence  
24 clearly supports the utilization of kyphoplasty in  
25 vertebral compression fractures, I believe that

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1 both basic and clinical science support this, I  
2 believe this for my patients, and I believe this  
3 currently is best practice. Thank you.

4 DR. MCNEIL: Thank you, Dr. Dohm.

5 Dr. Marks.

6 DR. MARKS: I'm Dr. Michael Marks, an  
7 orthopedic spine surgeon from Norwalk,  
8 Connecticut, and am also the immediate past  
9 president of the Connecticut Orthopedic Society.  
10 I'm speaking today on behalf of myself and all the  
11 patients I treat in my community, the spine  
12 surgeons of Connecticut, and I also work as a  
13 consultant for Kyphon. I own no stock in Kyphon  
14 or any other orthopedic device company. I do act  
15 as a consultant to other device companies besides  
16 Kyphon. I paid for my own transportation to  
17 today's meeting.

18 I am a community-based orthopedic spine  
19 surgeon based in Norwalk Hospital, a 220-bed  
20 institution in Norwalk, Connecticut that sounds  
21 very similar to Grand Junction, Colorado. I have  
22 been performing kyphoplasty since June of 2001 and  
23 in those years have operated on more than 250  
24 patients. I could present 250 anecdotal stories  
25 about my patients but we would probably be here

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1 all day, so instead I will address two specific  
2 topics.  
3 The first topic comes from an article  
4 by Crandall that was published in Spine in 2004  
5 that looked at acute spinal fractures and  
6 determined that fracture age does not affect the  
7 response to kyphoplasty. A summary of the study  
8 looked at 86 vertebral compression fractures in 47  
9 patients. 40 fractures were less than ten weeks  
10 old and 46 were greater than four months, with a  
11 mean age of 74, obviously Medicare age. The pain  
12 scores decreased equally in both groups.  
13 Vertebral body height can be restored in both of  
14 these groups but it seems to be better obtained in  
15 the acute group. There were no complications  
16 related to the procedure and kyphosal correction  
17 could be achieved in both of these groups.  
18 John Ledlie and his partner have  
19 produced a long-term follow-up of kyphoplasty,  
20 recently accepted for publication in the Spine  
21 Journal. They concluded that in two years  
22 patients demonstrated sustained benefit from  
23 kyphoplasty. In this study they investigated 117  
24 patients with 151 osteoporotic fractures. 77 with  
25 two-year follow-up with the mean age, again, of

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1 77. They found complete pain relief in 65 percent  
2 of these patients acutely and 86 by three to six  
3 months. They found a definite decreased need for  
4 pain medication, greater than 10 percent height  
5 was restored in 90 percent of fractures, and this  
6 height restoration was maintained after two years,  
7 and they found no complications associated with  
8 it.  
9 They also interestingly looked at  
10 ambulatory status, which I think is definitely one  
11 of the questions before us today with respect to  
12 mobility, and they found that the mobility to  
13 fully ambulate increased from 44 percent  
14 preoperatively to 85 percent at one week and 88  
15 percent at two years.  
16 To sum up, kyphoplasty in my practice  
17 works extremely well. I like Dr. Dohm have many,  
18 many patients and their families that come thank  
19 me for doing something to benefit their family  
20 member. It works well in both acute and chronic  
21 fractures to decrease pain and achieve some  
22 correction of vertebral body collapse, which  
23 obviously as an orthopedic surgeon is one of the  
24 tenets that I was taught early on. The beneficial  
25 results of kyphoplasty definitely improve

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1 functional status on a long-term basis. I want to  
2 thank you for allowing me to present today.  
3 DR. MCNEIL: Thank you very much,  
4 Dr. Marks. Dr. Talmadge.  
5 DR. TALMADGE: Good morning. I am  
6 Karen Talmadge, and my financial interest is that  
7 I am the chief science officer for Kyphon. I want  
8 to summarize how the scientific literature answers  
9 the panel's questions on the use of kyphoplasty.  
10 As background, my Ph.D. came from the department  
11 of biochemistry and molecular biology, and I've  
12 conducted post-doctoral research in other labs and  
13 I have been involved in the science of kyphoplasty  
14 since 1992.  
15 As you've heard from Dr. Gold,  
16 osteoporosis creates multiple health effects  
17 independent of pain. Patients with acute and  
18 painful vertebral fractures who are managed  
19 nonoperatively have poorer functional outcomes and  
20 remain impaired five years post diagnosis.  
21 As you've heard from Doctors Belkoff  
22 and Lieberman, the spinal deformity continues to  
23 get worse because each uncorrected compression  
24 fracture increases the risk of further fracture  
25 due to changes in the mechanics of the spine.

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1 As Dr. Jolivette has noted, there are  
2 now 28 balloon kyphoplasty studies involving 1,510  
3 patients. Eight of these studies showed marked,  
4 sustained and significant improvement with chronic  
5 fractures. 14 show the same marked, sustained,  
6 consistent improvement with acute fractures. Due  
7 to the similarity of outcomes, I will not  
8 distinguish them. Taken together, these studies  
9 show significant improvements in every clinical  
10 end point from the earliest time, seven days,  
11 sustained out to two years. This sharply  
12 contrasts with the literature on outcomes of  
13 nonoperative care for patients with osteoporotic  
14 compression fractures. This literature provides  
15 strong evidence that balloon kyphoplasty is  
16 superior to nonoperative care in the short term.  
17 The two concurrently controlled studies  
18 discussed by Dr. Cher show that pain and function  
19 are improved after kyphoplasty while pain and  
20 function when managed nonoperatively drops, and  
21 the subsequent fracture rate is significantly  
22 lower with follow-up at six months.  
23 The other 25 studies show the same  
24 consistent benefits. I apologize but part of my  
25 slides don't appear to be showing up, so it



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1 confused me a little bit.  
2 Similarly, ten studies provide strong  
3 evidence that the benefit is maintained long-term.  
4 The scientific data should provide this panel with  
5 a high confidence that the balloon kyphoplasty  
6 studies are valid. Among the three published  
7 trials are the two (inaudible) studies and the  
8 multicenter study described by Dr. Garfin. There  
9 are 13 additional single-center prospective  
10 studies. 27 studies address short-term outcome,  
11 ten address long-term, and the studies use seven  
12 different effectiveness measures.  
13 The panel can have high confidence that  
14 the scientific data on short-term outcomes are  
15 valid. The two concurrently controlled studies  
16 show superiority and the remaining 25 studies are  
17 consistent, including 16 studies that measure  
18 ambulation and other functional status.  
19 The panel can have the same high  
20 confidence in the scientific data of valid  
21 long-term, as the ten studies are consistent with  
22 each other and with the studies showing short-term  
23 benefits and (inaudible).  
24 Based on this literature, the panel can  
25 have high confidence that kyphoplasty will

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1 positively affect ambulation, functional status  
2 and vertebral height short term as well as long  
3 term. The risk of significant adverse events in  
4 all of these studies is low, 0.5 percent. There  
5 are no studies addressing mortality, but there  
6 were no perioperative deaths in this clinical  
7 literature, and given that nonoperative care is  
8 associated with excess mortality and increased  
9 spine deformity, the panel can expect kyphoplasty  
10 will reduce mortality based on its safety and in  
11 conjunction with its ability to reduce  
12 (inaudible).  
13 The key question for the panel is, will  
14 kyphoplasty produce a clinically meaningful net  
15 health benefit for patients with vertebral body  
16 compression fractures compared to nonoperative  
17 care? The clinical literature is clear. Patients  
18 treated nonoperatively get worse. Patients  
19 treated with kyphoplasty get better and stay  
20 better.  
21 Doctors Dohm, Marks and Garfin have  
22 confirmed that these results can be generalized to  
23 the Medicare population and to community  
24 providers.  
25 We appreciate the chance to provide an

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1 overview of the kyphoplasty issues at this  
2 meeting. In further support, we submitted a more  
3 detailed analysis of the clinical research in  
4 writing, and we are pleased to answer any  
5 questions the panel may have about our verbal or  
6 written remarks.  
7 DR. MCNEIL: Thank you very much.  
8 Dr. Evans.  
9 DR. EVANS: Hello. I'm Avery Evans,  
10 I'm an associate professor of radiology and  
11 neurosurgery at the University of Virginia. By  
12 way of disclosure, I paid for my own travel  
13 arrangements. I do receive royalties from Cook  
14 and Cardinal on various vertebroplasty products.  
15 I would like to start off by echoing  
16 Dr. Belkoff's comments and frustrations regarding  
17 the lack of prospective randomized controlled  
18 trials when it comes to vertebroplasty. I would  
19 like to note, though, that if you look in the  
20 literature, fewer than five percent of surgical  
21 procedures are ever subjected to that level of  
22 scrutiny.  
23 Secondly, I would say it's not  
24 necessarily for lack of effort that there are no  
25 prospective randomized controlled trials. Over

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1 six years ago in Tampa, Florida, my research group  
2 designed a randomized controlled trial, and over  
3 the course of a year we tried to enroll patients  
4 who would be randomized to vertebroplasty or to  
5 conservative therapy. I interviewed over a  
6 hundred patients. I got two patients to say that  
7 they would be in the trial. One patient  
8 randomized to vertebroplasty, she went home that  
9 afternoon with no pain, fully ambulatory. The  
10 second patient randomized to medical therapy, she  
11 went to bed rest. She died three weeks later from  
12 complications related to bed rest. In the course  
13 of a year, interviewing a hundred patients, I  
14 could not get enough patients. And that was six  
15 years ago, I was the only patient in town who did  
16 vertebroplasty. These days if you try such a  
17 setting, patients will go across the street to  
18 somebody who will do it.  
19 So, we couldn't do that study and we  
20 did this one instead. This is 72 patients that we  
21 evaluated prospectively with a validated  
22 questionnaire. 161 patients were interviewed and  
23 72 consented to complete the study. Patients then  
24 completed a questionnaire and were reassessed at  
25 one week and six weeks after vertebroplasty, they

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1 served as our controls. We measured differences  
2 in self-reported pain and distress after  
3 vertebroplasty, differences in pain and distress  
4 at the first and second follow-up intervals, and  
5 mean scores for 24 activities of daily living  
6 based on a one to five scale. The mean age of the  
7 patients was 74 years, 80 percent were female.  
8 None of these patients suffered symptomatic  
9 complications, nine percent had asymptomatic  
10 leakage of PMMA into adjacent soft tissues.  
11 Results, visual analog scale, the mean  
12 pain reported pre-vertebroplasty was 5.8,  
13 post-vertebroplasty was 3.5, and that was  
14 significant as you can see. The reduction  
15 persisted between the first and second follow-ups.  
16 The ability to perform all ADLs was increased  
17 without pain or with little pain for all  
18 activities except for doing gardening. The  
19 majority of this improvement was sustained and  
20 this data is seen graphically. You can see that  
21 pain on the visual analog scale averaged 5.8 and  
22 that decreased to 3.5, and that was a stable  
23 decrease between the first and second follow-ups.  
24 On the adjectival scale you see the same thing,  
25 all these results were statistically significant.

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1 Activities of daily living, such things  
2 as wash dishes, drive an automobile, climb stairs,  
3 lift light objects, lift heavy objects, you can  
4 see the difference between the baseline, which was  
5 the unshaded area, and then the follow-up number,  
6 and every single activity increased significantly  
7 between the vertebroplasty and the first  
8 follow-up, with the exception of doing gardening.  
9 So in conclusion, in this prospective  
10 nonrandomized trial, vertebroplasty resulted in a  
11 substantial lasting reduction in pain and  
12 improvement to perform activities of daily living.  
13 Thank you.

14 DR. MCNEIL: Thank you very much.

15 Dr. Mathis.

16 DR. MATHIS: Hello, I'm John Mathis.

17 Thank you for the opportunity to come. I would  
18 like to just first say I'm sorry that I only get  
19 four minutes, and Dr. McNeil, because I speak so  
20 slowly, I really think I should get ten. I have  
21 had the opportunity to work for Kyphon, Orthopeda,  
22 Stryker, all of which I had financial  
23 relationships with. Stryker paid for my travel.  
24 I represent the American Society of Spine  
25 Radiology, and I'm a professor and chairman of the

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1 department of radiology at Virginia College of  
2 Osteopathic Medicine in Blacksburg, Virginia.  
3 My research colleague, Steve Belkoff,  
4 we've written one book, have another book in  
5 print, 18 peer reviewed articles on vertebroplasty  
6 and 14 chapters. I was fortunate to work with  
7 Dr. Jensen, Dr. Kallmes, Dr. Evans, we introduced  
8 vertebroplasty in the United States, and I've been  
9 to the University of Maryland and Johns Hopkins.  
10 The things I want to talk to you about  
11 today are a little different from the other people  
12 because basically they stated very well the fact  
13 that we think this works. This is cement  
14 augmentation of bone fracture, it does appear to  
15 relieve pain in the appropriate set of patients.  
16 What I think is misstated here and I think is  
17 taken awry is, is there vertebroplasty and  
18 kyphoplasty. I don't even think kyphoplasty  
19 should be a term, I think it should be balloon-  
20 assisted vertebroplasty because both of them  
21 relieve pain based on the augmentation with  
22 cement. If you take out a gall bladder, it  
23 doesn't matter whether you take it out with a  
24 scalpel or with a laser; at the end of the day  
25 it's the gall bladder removal that makes the

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1 difference. At the end of the day, it's the  
2 cementation of the bone, and that's the only way  
3 we've found so far to make the pain go away.  
4 And you hold a critical opportunity to  
5 do damage or to do positive to this whole process,  
6 and that is how you decide to reimburse for these  
7 procedures. Everyone here has spoken in favor of  
8 the fact that it seems that this relieves pain  
9 acutely. But if you decide to reimburse a dollar  
10 for the vertebroplasty and three dollars for what  
11 is called kyphoplasty or balloon-assisted  
12 vertebroplasty, as Dr. Belkoff has already said,  
13 there are multiple other ways to get height  
14 restoration, including vertebroplasty.  
15 But if you reimburse a dollar for  
16 vertebroplasty and three dollars for kyphoplasty,  
17 you will decide whether or not physicians use one  
18 or the other, because if it takes no more time and  
19 as past representatives have already said, there  
20 is no difference in the time to do the operation,  
21 then I won't do vertebroplasty anymore, I will do  
22 kyphoplasty, because in the same amount of time in  
23 my lab I can make three times as much money. You  
24 will decide where we go forward and whether or not  
25 we get the appropriate research that we need. And



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1 right now, what we need is when do you use  
2 kyphoplasty or when do you use vertebroplasty,  
3 what patients are appropriate and what patients  
4 are not. Patients selection is key to this whole  
5 process. I thank you so much for being here, your  
6 involvement in this process is very, very  
7 important. Thank you.  
8 DR. MCNEIL: Thank you, Dr. Mathis.  
9 And finally, Dr. McKiernan.  
10 DR. MCKIERNAN: I have no conflict of  
11 interest to disclose and my employer, Marshfield  
12 Clinic, paid for my transportation costs.  
13 Today we have heard reports of dramatic  
14 pain relief following vertebral augmentation and  
15 seen images remarkable showing height restoration.  
16 As you conduct your inquiry into the quality of  
17 the scientific evidence pertaining to  
18 vertebroplasty and kyphoplasty, I ask you to  
19 consider the following three issues.  
20 This is a standing lateral radiograph  
21 of a two-week-old osteoporotic vertebral  
22 compression fracture on the left slide, and  
23 moments later the same fracture in a supine  
24 position. This vertebra demonstrates dynamic  
25 mobility. This is a standing lateral radiograph

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1 of a 14-month-old fracture and moments later the  
2 same fracture in the supine position. This  
3 vertebra defines that mobile fractures contain  
4 clefts. And finally, this vertebra plain will  
5 illustrate intravertebral void in the supine  
6 position. Clinical researchers must therefore  
7 account for that portion of the vertebral height  
8 restoration due to mobility before it can be  
9 ascribed to any other mechanism.

10 There are several methods for reporting  
11 vertebral height restoration. If a four-  
12 millimeter depression superior end plate is  
13 followed by a three-millimeter restoration, one  
14 could say that this three millimeters constituted  
15 a 75 percent vertebral height restoration. Using  
16 this same method, if a 25-millimeter depression  
17 superior end plate is followed by a five-  
18 millimeter elevation, compared to the greater  
19 elevation, this reporting method would assign a 20  
20 percent height restoration. This reporting method  
21 termed percent of lost height restored with  
22 inflation numerically favors a small magnitude of  
23 height restoration in myelofractures.

24 Unfortunately this reporting method is still  
25 commonly used.

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1 Finally, journal editors should require  
2 disclosure of anterior, middle and posterior  
3 vertebral heights when reporting height  
4 restoration because a vertebra may fail in the  
5 middle portion, and yet there may be no change in  
6 anterior height. Even with complete height  
7 restoration, there's been no net change in the  
8 anterior vertebral height or angle. Without  
9 knowledge of all vertebral heights, claims of  
10 vertebral height restoration solely based on  
11 middle height may not be clinically relevant.  
12 In the interest of time, I will skip  
13 this.  
14 So, what is the quality of the  
15 scientific evidence addressed in our literature?  
16 I call your attention to this article, published  
17 last month in the Journal of Bone and Mineral  
18 Research. The authors conclude that kyphoplasty  
19 reduces pain and improves function, a conclusion I  
20 think is supported by facts with which I don't  
21 agree. Unfortunately, the authors report on only  
22 middle height and use the percent of lost height  
23 restored method that we previously discussed.  
24 In the discussion section, these  
25 authors perpetuate the misconception that mobility

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1 is only transiently seen in only very recent  
2 vertebral compression fractures and cite less than  
3 four weeks old. The support for this is  
4 apparently found in references 35 and 36, which  
5 are from my group. We do not perform kyphoplasty,  
6 we perform vertebroplasty, and our average  
7 fracture age is four months. The notion of less  
8 than four-week-old fractures appears nowhere in  
9 the text of either of our articles.  
10 Finally, towards the end of the  
11 discussion section, the authors provide five  
12 references to support their assertion that pain  
13 relief and vertebral height restoration are not  
14 correlated in the vertebroplasty literature. Both  
15 references 25 and 26 have no mention of  
16 vertebroplasty in their titled text. 34 is an  
17 ex vivo evaluation of the Kyphon balloon, and 39  
18 is a study of epidural cement leak damage, and 40  
19 is a review article that doesn't address the issue  
20 of pain reduction.  
21 In summary, I ask the committee to  
22 consider the following points when deliberating  
23 the quality of the scientific evidence. Is the  
24 issue of dynamic mobility rigorously addressed?  
25 Is their accountability in vertebral morphometry?

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1 Is there integrity in reporting? Are the results  
2 clinically relevant, is the procedure cost  
3 effective, is it science or is it marketing?  
4 DR. MCNEIL: Thank you very much,  
5 Dr. McKiernan. Dr. Phurrough, did you want to  
6 make a comment?  
7 DR. PHURROUGH: Yes. Just a comment,  
8 if I can get the microphone turned on. Thank you.  
9 I apologize for not mentioning this at the  
10 beginning of this session. The purpose of this  
11 panel is to address the evidence and to make  
12 recommendations to CMS as to the quality of the  
13 evidence, and this panel will not make  
14 recommendations as to whether we should or should  
15 not change any payment methodology, whether we  
16 should or should not make a coverage decision,  
17 whether vertebroplasty should be reimbursed at a  
18 higher level than kyphoplasty. None of these  
19 questions are pertinent for this particular panel.  
20 The panel is solely to answer the question, what's  
21 the quality of evidence and what does that  
22 evidence show.  
23 So as we go throughout the day this  
24 afternoon and have discussions, we won't be  
25 addressing those questions. Even though those are

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1 important questions to be addressed, those are in  
2 the purview only of CMS internally and we will  
3 look at the recommendations on the evidence that  
4 the panel makes today and use that as we make  
5 determinations in the future about coverage and  
6 payment. I just want to make sure that is clear,  
7 and I apologize for not making that clear earlier.  
8 DR. MCNEIL: So we have three public  
9 speakers, Miss Haley, Domescus and Lavasseur. So,  
10 you will each have two-and-a-half minutes and  
11 maybe the first speaker is here, Mary Haley, and  
12 if Cindy Domescus could step up front so she will  
13 be ready.  
14 MS. HALEY: I don't think Cindy is  
15 going to speak after all.  
16 DR. MCNEIL: Okay.  
17 MS. HALEY: I'm Mary Haley, and I'm the  
18 vice president of reimbursement for Kyphon.  
19 The questions today relate to both  
20 vertebroplasty and kyphoplasty in relation to  
21 conservative care. I have had the opportunity to  
22 work with the local Medicare directors throughout  
23 the past years for coverage and one of the  
24 opportunities I have had is to work with the  
25 medical directors, the staff members, clinicians

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1 in establishing coverage policies at the local  
2 level, and there is one policy that was just  
3 published recently that I think brings some of  
4 these points home, both on conservative care, but  
5 more importantly, for the treatment of both  
6 vertebroplasty and kyphoplasty.  
7 They recognized that delay of either  
8 treatment pending response to medical management  
9 may not be in the best interests of the patient,  
10 and in those instances where the provider feels it  
11 is medically reasonable and necessary to proceed  
12 to treatment, either procedure immediately or  
13 within a brief time after the vertebral fracture  
14 occurs, the medical record must clearly document  
15 the justification for the decision. This is one  
16 of the Medicare providers that covers 11 states  
17 that has acknowledged the fact that the medical  
18 management may not be in the best interest of the  
19 patient and that either procedure may actually be  
20 considered good care. Thank you.  
21 DR. MCNEIL: Thank you very much. Is  
22 Brooke Lavasseur here? I guess everything has  
23 been said then. Okay, let's see. At this point,  
24 it's probably reasonable to break rather than to  
25 start asking questions of the presenters. Let's

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1 do the following. We will reconvene at 12:30 and  
2 then from 12:30 until about one we will ask all of  
3 the speakers or some of the speakers, we'll ask  
4 them questions, really clarifying questions about  
5 their presentations. Subsequent to that, starting  
6 at one o'clock, the panel will largely deliberate  
7 internally, with maybe an occasional question from  
8 the audience, but I don't really expect a lot of  
9 interaction between us and you after one o'clock  
10 or shortly thereafter. So with that in mind then,  
11 I would encourage the panel over lunch to get the  
12 questions sharply in order, and we will start back  
13 at 12:30. Thank you.

14 (Luncheon recess.)

15 DR. MCNEIL: Welcome back everybody, I  
16 hope you had a relaxing lunch, a little bit less  
17 fast, a little bit slower than the morning.  
18 Before we reconvene, I'd like to ask  
19 Jonathan Weiner to introduce himself, he came in a  
20 little bit late.

21 DR. WEINER: Hi. I'm Jonathan Weiner,  
22 a professor at Johns Hopkins School of Public  
23 Health. Sorry I was late, but the dog didn't like  
24 my car. Anyway, I have no conflicts of interest.

25 DR. MCNEIL: Thanks, Jonathan. Here we



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1 are. The idea now is for us to ask the panelists  
2 for clarification of any issues that we didn't  
3 have a chance to after their discussions and at  
4 the end of that time, we will start our  
5 deliberations. So, who would like to go first?  
6 MR. QUEENAN: This question would be  
7 directed to any of the speakers who are  
8 practitioners who use both of the two procedures  
9 being discussed here, and the question is, when  
10 you have a particular patient, how is it that you  
11 decide which procedure to use?  
12 DR. LIEBERMAN: I guess I'll lead off  
13 on that. I'm Isador Lieberman, from the Cleveland  
14 Clinic. There are a number of issues that go into  
15 the decision-making that I look at, the first of  
16 which is the chronicity of the fracture; the  
17 second of which is the duration; third, the  
18 underlying physiology or metabolic process, is it  
19 tumor or osteoporosis; the fourth of which is the  
20 patient itself, what does the patient really need  
21 for that?  
22 If they've got just a super end plate  
23 fracture which hasn't really collapsed down and  
24 they're what I call an at-risk patient, and it's  
25 at the thoracolumbar junction, then some kind of

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1 vertebral augmentation in the form of a  
2 vertebroplasty may be the appropriate way to go  
3 with it. If on the other hand it's a complex  
4 deformity, if it's a tumor patient with a big hole  
5 in there already, if I'm concerned about where  
6 that cement is going to flow and it's  
7 significantly collapsed, then I will want to  
8 reduce the anatomy, restore the alignment, create  
9 that cavity, and then fill that vertebral body up  
10 for biomechanical and deformity purposes.  
11 DR. DOHM: I'm Mike Dohm again. In  
12 private practice in Colorado, for me it's evolved  
13 to the point where patients that can't undergo a  
14 general anesthetic for vertebroplasty, if they're  
15 medically unable to tolerate a procedure like  
16 that, I still don't feel comfortable doing  
17 kyphoplasty under just a local. At this point I  
18 have colleagues that do that all the time very  
19 successfully, it's just personal preference. But  
20 in decision and my operative approach, for those  
21 patients who have had multiple lesions in the past  
22 and it's just a palliative procedure, I feel much  
23 more comfortable having them go the vertebroplasty  
24 route. If they're a very active individual, if I  
25 think that I can intervene with reduction of

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1 fracture and then fixation, that's when I perform  
2 a kyphoplasty.  
3 DR. HIRSCH: Josh Hirsch, Boston. I  
4 came to kyphoplasty through vertebroplasty, I  
5 believe they are both equally effective, and I  
6 believe the complication is equal as to both  
7 procedures under anesthesia that is similar to  
8 conscious sedation, unless the anesthesiologist  
9 prefers them to undergo general anesthesia. To  
10 that end, I think that the times that I use  
11 kyphoplasty are when I really, really want to push  
12 for height restoration. I think that as previous  
13 speakers, when the patient is frail, et cetera, I  
14 lean much more towards vertebroplasty because I  
15 can get in there quicker.  
16 DR. PHURROUGH: Before you leave, why  
17 would you want to do kyphoplasty when you really,  
18 really wanted to do height restoration? What  
19 leads you to want to do height restoration?  
20 DR. HIRSCH: That's a very complex  
21 question that I try to answer all the time, and  
22 I'm still working on it in my head. The work by  
23 Dr. McKiernan and colleague Tom Budzuski stressed  
24 that with vertebroplasty, as has been my personal  
25 observation, you can achieve outstanding height

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1 restoration with percutaneous vertebroplasty. To  
2 me the jury is still out on this issue of the  
3 value of sagittal realignment. However, I think  
4 that at times when there's a compelling argument  
5 for trying to reduce the kyphosis you may want to  
6 do it in that fashion.  
7 I will further share with the group  
8 that in my experience, prior to doing  
9 kyphoplasties I had done many, many, many  
10 vertebroplasties, and the pain relief does allow  
11 patients to stand up straighter by itself, and I  
12 think that in and of itself precludes the  
13 kyphoplasty. As I said in my comments,  
14 vertebroplasty and kyphoplasty are sort of a  
15 continuum and both work spectacularly well in this  
16 population, so vertebroplasty would continue to be  
17 the primary treatment.  
18 MS. STARMANN-HARRISON: What percentage  
19 of your patients receive each type of procedure?  
20 DR. HIRSCH: I haven't regularly looked  
21 at that, it's a valid question. I would suspect  
22 it's two-thirds vertebroplasty and one-third  
23 kyphoplasty and its equivalents.  
24 DR. MCNEIL: I'm sorry, Josh, could I  
25 just follow up? I'm still a little bit confused

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1 about this height restoration. We learned this  
2 morning that it's three millimeters. So, of the  
3 third of your procedures where you do kyphoplasty  
4 instead of vertebroplasty, or whatever that number  
5 you just gave was, what proportion of that group  
6 is for height restoration and what are the  
7 indications for the others?

8 DR. HIRSCH: Say that one more time.

9 DR. MCNEIL: Well, I think you said a  
10 third of your patients have kyphoplasty; and then  
11 you also said that you push for kyphoplasty when  
12 you're looking for height restoration, and Steve  
13 asked you under what circumstances that was the  
14 case. Given that the height restoration is three  
15 millimeters or so, at least that's what we heard  
16 this morning, that would apply to one-third of the  
17 patients, and that one-third of the patients is a  
18 fraction, then, that really need that three  
19 millimeters. What do the others need?

20 DR. HIRSCH: That's fair. Of course  
21 it's fair. Let me be clear about this. There  
22 have been many recent advocates for treatment  
23 with kyphoplasty over the years. I believe  
24 vertebroplasty and kyphoplasty to be equally safe  
25 and effective treatments, particularly for pain.

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1 In my practice, therefore, I will limit the  
2 patients that I believe will benefit from height  
3 restoration, and also using kyphoplasty for  
4 myeloma preferentially. I think that, again, the  
5 issue of height restoration is a complex one, and  
6 I don't mean to sound redundant on this point, in  
7 that the patient-physician interplay is extremely  
8 important, again, and Tom Budzuski has an article  
9 about this with vertebroplasty, I think showing  
10 108 percent of post-treatment height versus  
11 preliminarily, meaning I think there's further  
12 stretching possible with vertebroplasty.  
13 I believe in terms of, however, the  
14 likelihood of a priori thinking you're going to  
15 achieve height restoration (inaudible) other  
16 products, at least in my mind afford a greater  
17 opportunity to achieve that height restoration. I  
18 believe in my practice, some of the early work was  
19 done using portable C arms, et cetera, but I  
20 really push these balloons and push the  
21 treatments. But I think this is something that  
22 should be studied further actually, because this  
23 issue of restoration is driving a lot of what we  
24 do.  
25 DR. MCNEIL: Further questions?

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1 DR. ONDRA: I was wondering about  
2 alignment locally, regionally and globally, and  
3 that was my question earlier to Dr. Lieberman,  
4 does height restoration and the importance of that  
5 in any way translate to kyphosis restoration at a  
6 body level or a regional level? And before we say  
7 that this is it, I want somebody to make it clear  
8 to me what data do we have to show a benefit over  
9 vertebroplasty.

10 DR. HIRSCH: I would answer in two  
11 ways. One of the presenters, and I can't remember  
12 which, stressed very clearly the importance of how  
13 you measure height restoration, so I would  
14 encourage in future studies us to consider which,  
15 and that would be relevant to determine  
16 (inaudible) to the vertebral body.  
17 To the other point, I think it is clear  
18 to me that any of the family of treatments for  
19 pain will correct what I think you're calling  
20 global kyphosis. In my opinion, patients who are  
21 hunched over are often in that position because  
22 they are in terrible pain. So relieving that pain  
23 will help, and I don't believe most people in this  
24 room, at least on this side, dispute any of these  
25 procedures do, and I think often will correct a

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1 lot of the kyphosis, and I think that's valuable.  
2 DR. RESNICK: Just to clarify an issue  
3 in my mind, we have as our charge to evaluate the  
4 literature as to whether or not either of or both  
5 of these treatments are effective for relieving  
6 pain following vertebral body fractures, and so  
7 the comparison theme is, I don't know why we're  
8 dwelling on it. And with the discussions of the  
9 subsequent vertebral fractures aside, it seems to  
10 me that in terms of patient outcomes and  
11 functional outcomes from either or both of these  
12 procedures, the question is whether you believe  
13 that either kyphoplasty or vertebroplasty have  
14 demonstrated adequate efficacy for relieving pain.  
15 DR. HIRSCH: I'm delighted to retake my  
16 seat.  
17 (Laughter.)  
18 DR. MCNEIL: Well, one thing I would  
19 like to be particularly careful of, since we only  
20 have a limited number of minutes for questions, so  
21 that we don't need to hear the same answer from  
22 several people. That would not aid us in our  
23 deliberations.  
24 DR. DOHM: If I can just speak to  
25 outcomes, as far as the outcomes question, you



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1 know, again, after Dr. Weinstein's discussion in  
2 the '90s and our societies looked at the outcomes  
3 and guidelines and the algorithms. In my  
4 practice, daily I look at Maine analog scales, I  
5 look at some form of measurement that most  
6 patients do. And what's unfortunate is I'm in  
7 private practice, and as a clinician-scientist,  
8 fewer than ten percent of us are  
9 clinician-scientists because with the demands of  
10 practice, it is so difficult to be able to report  
11 to you in some sort of a written format that shows  
12 how the patients do.  
13 So I can look at other people's study  
14 and give you my anecdotes, but I would be more  
15 active if I had the opportunity, which is, you  
16 know, talking to these patients and looking at  
17 their pain scales and looking at their forms of  
18 reports, their activities of daily living.  
19 I looked at 50 or 60 patients of mine  
20 that I presented to our community about two years  
21 ago, and we found that two to four percent of  
22 those were tumor, the rest were  
23 osteoporosis-related fractures, and in terms of  
24 activities of daily living, everyone did better,  
25 about 85 percent or better. If we asked someone

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1 whether they wanted to have the procedure or not,  
2 again, it was about 85 percent that would have  
3 undergone the procedure again, and I know they had  
4 some statistically significant changes in their  
5 lives. I mean, that's what's obvious. The hard  
6 part is really measuring that in terms of getting  
7 something to compare it to. I, again, I follow  
8 these patients with nonoperative care and again, I  
9 operate on fewer than ten percent of the people  
10 that I see in my clinic. I think I've got like  
11 50,000 patient hours in the last 12 years, and  
12 these patients do a lot better with that, and I  
13 can show them that, compared to nonoperative  
14 treatment.

15 DR. MCNEIL: Dr. Weinstein?

16 DR. WEINSTEIN: I guess I was  
17 interested in more of a process issue from the  
18 patient's perspective. Radiologists do patient  
19 care differently than orthopedic surgeons and  
20 neurosurgeons, and I guess one of the problems I  
21 see in the literature is this follow-up issue.  
22 And I'm wondering if there is a difference in  
23 process of care for patients based on discipline.  
24 We don't talk a lot about it but I think some of  
25 the literature is limited by the practice style,

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1 the ability to collect data in different ways,  
2 because as you alluded to, it's not very easy to  
3 do. And I wonder what our obligation is to  
4 undertake these things, what our obligation is to  
5 see patients, evaluate them and then to collect  
6 information longitudinally in what way, given the  
7 different disciplines. I think the panel would  
8 like to understand how you do that.  
9 DR. DOHM: I think this should be a  
10 standard of care and I'm just surprised and  
11 dumbfounded that this isn't a standard of care. I  
12 have to find IRB approval just like anyone  
13 involved in the study, and then many people don't  
14 participate because it's very onerous, so it's not  
15 a standard of care yet, but I hope to God it will  
16 be in the next ten years.  
17 I know from being involved with the  
18 American College of Surgeons, the VA system, which  
19 is now 132 hospitals, are participating in the  
20 national surgical quality improvement project,  
21 they all have to do that to have the same  
22 electronic medical record. The American College  
23 of Surgeons has bought this and is trying to move  
24 it into the private sector but running into  
25 difficulties. CMS is trying to do the (inaudible)

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1 project, that's another problem. We talked about  
2 our own registries, that's another problem. So  
3 none of us seem to collaborate well enough  
4 together to get preoperative data, hospital data  
5 and postoperative data, and that would be my hope,  
6 that we could all work together to do that.  
7 DR. MCNEIL: Could I just clarify that?  
8 I didn't hear that as the question, I heard the  
9 question slightly differently. I thought I heard,  
10 why are there differences in practice style post  
11 whatever, and why aren't the individual  
12 specialties or physicians within those specialties  
13 responsible in the same fashion for collecting  
14 those data to make sure that what they say is  
15 really correct. Is that where you were going?  
16 DR. WEINSTEIN: It's really, there is  
17 this issue of cross-disciplinary, and I think we  
18 would be at fault for not looking at that. And  
19 how do you get your patients in your clinical  
20 practice? A radiologist might get them by  
21 referral or a different way, and patients get lost  
22 in that process and therefore get lost in the  
23 collection of data, and then it's passed on to the  
24 studies that we've seen. I suppose if I heard Dr.  
25 Hirsch versus Dr. Lieberman, I would get a

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1 different answer of how they get their patients  
2 and how they follow that patient.

3 DR. DOHM: In my community, I am a  
4 primary care doctor and I see that patient and  
5 family members and everyone else from the time  
6 they're born until they are dead, so I'm like a  
7 family doctor. The interventional radiologists  
8 see them for this period of time because of the  
9 referral for anesthesia or physical medicine  
10 rehabilitation.

11 DR. MCNEIL: Did you have a different  
12 answer?

13 DR. MCGRAW: Hi, I'm Dr. Kevin McGraw,  
14 an interventional radiologist. As an  
15 interventional radiologist, we actually have a  
16 very busy clinical practice. Maybe ten years ago  
17 the interventional radiologists relied on  
18 referrals. Now there is a paradigm shift within  
19 our specialty to assume more of a clinical  
20 responsibility to see patients in an office  
21 setting, admit patients post procedurally, see  
22 them in follow-up and provide continued  
23 longitudinal care. This is something we do  
24 routinely in our practice, and I think I speak for  
25 the majority of interventional radiologists and

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1 interventional therapy radiologists that we now  
2 have a dedication to clinical patient care and  
3 seeing them in an office setting and providing  
4 appropriate treatment. All of our patients for  
5 vertebral augmentation are followed out to one  
6 year post procedurally, and I think the majority  
7 of my colleagues also provide the appropriate care  
8 with that.  
9 That's why, you know, I had a published  
10 study with 100 patients with a mean follow-up of  
11 22 months that was part of the, it's in your  
12 literature packet. So I think there is a  
13 misconception about radiologists and  
14 interventional radiologists, and intervention  
15 neuroradiologists, because we do provide clinical  
16 care.  
17 DR. MCNEIL: Dr. Resnick?  
18 DR. RESNICK: I just have a question  
19 for Dr. Mark about the technology assessment. In  
20 every paper that has been reviewed, there has been  
21 a demonstrated positive effect of these  
22 augmentation procedures, and that's been  
23 consistent from European studies, radiology  
24 studies, orthopedic studies, et cetera. There  
25 have been today referenced three comparative

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1 studies with subsequent control, and really the  
2 only difference in the outcomes of those  
3 comparative studies was the duration of the  
4 effect. The Diamond study had a very short  
5 duration effect and the other two studies had much  
6 longer duration of effect.  
7 Your conclusion at the end of your  
8 presentation is that the, you recommended that the  
9 procedure not be approved or not be supported  
10 through Blue Cross Blue Shield, and I was  
11 wondering how you came to that conclusion after  
12 reviewing the literature that we all heard.  
13 DR. MARK: First of all, the review has  
14 been updated since, about eight months ago, and  
15 the additions to the literature are two-thirds of  
16 the observational studies. At the time of our  
17 initial review, there was only the one  
18 observational comparative study by Diamond which  
19 as you recall, showed a difference in the 24-hour  
20 outcome which dissipated as the control group got  
21 better at six weeks.  
22 And I think part of the difficulty in  
23 one issue that has been, I wish maybe there was  
24 another person here to try to elucidate that  
25 issue, is the natural history of the types of

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1 patients that are being selected to have that  
2 procedure, and that in our review and some of the  
3 background material that you have in the report  
4 and the additional background piece I did, I kind  
5 of tried to make an attempt to elucidate what the  
6 natural history of this condition is and kind of  
7 concluded that what I had at hand was of limited  
8 utility because of issues of comparability. These  
9 patients that had a workup, there were differences  
10 in clinical presentation and then they had been  
11 selected.  
12 So the caution, I guess, and I think  
13 our own medical panel which reviewed this  
14 evidence, I think did weigh rather impressive  
15 changes in visual analog scales and other  
16 functions against the type of study design that  
17 was done. So the question was, can the magnitude  
18 of the effects be explained by all the other  
19 problems that we know about observational studies,  
20 such as just placebo effect. There is an issue  
21 with natural history, there's a waxing and waning  
22 and regression to the mean effect of when patients  
23 present to care. And I think the important issue  
24 was weighing, exactly weighing those two issues,  
25 and I think the decision kind of came down to, do



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1 we really have a good handle on how these patients  
2 are selected out of all the patients that have  
3 back pain and, you know, basically that issue. We  
4 don't really have a good handle to fully  
5 understand the natural history of the patients out  
6 of all the patients that have back pain, so it was  
7 a weighing of that.

8 DR. MCNEIL: Dr. Fendrick, did you have  
9 a question?

10 DR. FENDRICK: I think my question  
11 would be a higher level question, a 30,000-foot  
12 question to the practitioners and the supporters  
13 of this procedure. And I'm impressed by your  
14 dedication and compassion to the patients as I  
15 listen to the human side of this story. But  
16 having personally been embroiled in several  
17 interventions over the years that were accepted in  
18 observational studies without adequate controls,  
19 that yet, a few of those studies when RCTs  
20 eventually were done were found to not be there.  
21 I'm going to ask you basically, what kind of  
22 assurances can you give me or us that vertebral  
23 augmentation, given the lack of adequate  
24 controlled trials that you all admit to, will not  
25 turn out to be like internal mammary ligation, the

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1 gastric bubble, endoscopic meniscal repair for the  
2 knee, and I could keep going on and on and on, but  
3 examples where medical interventions have been  
4 widespread adopted and they've actually been shown  
5 to have limited benefit and in rare circumstances  
6 fatal, actually hurt patients in the end. And to  
7 specifically address this failure to be able to do  
8 the randomized trial, I think I need to hear a  
9 little bit more about the details of the  
10 practicality of not giving us the evidence that  
11 some of us might need to make an easier decision.  
12 DR. DOHM: I asked my patients that. I  
13 said, look, I'm going to go meet with these guys  
14 in the next month or so, or whatever, and I said  
15 what should I say to the people that are  
16 listening, for you the patient. I had a lady a  
17 couple weeks ago where her daughter says, you  
18 know, this is just amazingly different now in  
19 looking at my mother, the way she is now, getting  
20 out, doing things, compared to how it was before.  
21 And I hate the anecdotes, I really do.  
22 DR. FENDRICK: And I'll tell you, if  
23 there were studies 40 years ago that looked at  
24 women who underwent perithyroidectomy for  
25 asymptomatic hypercalcemia, so they were

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1 asymptomatic but they were saying they felt better  
2 and they would have it done again. So we all,  
3 many of us believe in the strength of the placebo  
4 effect, and I hope that you and the others --  
5 you're persuasive to an extent, but you can't tell  
6 me that your great hands, Michael Dohm, are enough  
7 to make those patients perfect.  
8 DR. DOHM: No. I'm just a person, I  
9 recommend Joe America I think, or Josephine  
10 America, and the thing is, when I see these  
11 patients, I think I have a pretty cultured mind  
12 for trying to look at it in an evidence-based  
13 fashion and with a good scaffolding. And I've  
14 given my best efforts to have an infrastructure of  
15 data collection, and I think I do this better than  
16 most private practices in the country, and I do  
17 have some supportive data.  
18 DR. FENDRICK: But it may not be good  
19 enough for me.  
20 DR. DOHM: Well, no, I understand that.  
21 But I'm saying also, I've evolved. So now I treat  
22 these patients, I also do injections of the spine,  
23 I also do rhizolysis to try to cure the pain. So  
24 I have a pretty good idea of classification  
25 categorization, and these patients do better, and

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1 I think the data does support that. Does it need  
2 more? We're just in the beginning.

3 DR. MCNEIL: Why don't we hear from the  
4 academic center? Cleveland does lots of studies.

5 DR. LIEBERMAN: Lots of studies, and I  
6 think we were also involved with the arthroscopic  
7 meniscal knee repair study and my recollection is  
8 that it is a good operation and it does work.

9 SPEAKER: Knee repair?

10 DR. LIEBERMAN: Knee repair, meniscal  
11 repair. We've got to define what we're looking  
12 at. You've got a room full of dedicated  
13 practitioners, as you pointed out, and the one  
14 thing that's stark to me is just the volume of  
15 patients that have been treated. These patients  
16 would not be coming back to us if this was a bad  
17 operation, if patients were dying, if they weren't  
18 doing any better. The biggest referral source for  
19 me is my previous patients. I don't know --

20 DR. FENDRICK: Didn't the same thing  
21 happen with hormone replacement therapy? I want  
22 you to raise the bar for me, please.

23 DR. LIEBERMAN: I showed you the  
24 results on 329 patients that were analyzed over  
25 and over again in as specific as we possibly can

00173

1 get, and to discount that evidence because it's  
2 not randomized controlled trials, I mean, look, we  
3 still have very good objective prospective  
4 evidence with pre-intervention baseline  
5 information, post-intervention information, that  
6 showed statistically significant improvements that  
7 were carried out to one year and to two years. We  
8 can see that with both vertebroplasty and with  
9 kyphoplasty in multiple other ventures that we're  
10 doing at this moment. So we are dealing with a  
11 much larger picture, you can't discount it. What  
12 you're effectively saying is, the glass is  
13 three-quarters full, let's empty the glass.  
14 DR. FENDRICK: Let's agree on that. I  
15 like the three-quarters full, don't get me wrong.  
16 Tell me a little more about your experience of  
17 this impossibility of doing the adequate control.  
18 DR. LIEBERMAN: There have been a  
19 number of issues, and over lunch a number of us  
20 got together and we said let's go ahead and do it.  
21 But first and foremost right now is going to be  
22 the patients. These patients are going to come  
23 and they're coming for specific treatment. They  
24 come to me because they know that I was involved  
25 in developing the kyphoplasty and that's what I do

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1 and that's what they want. When I tell them that  
2 they're going to be randomized, they're going to  
3 have to do this paper work, they walk out the  
4 door, they walk down the street and they find  
5 someone in private practice who's not going to put  
6 them through all that. That's what's happening,  
7 that's what's unfortunate. We should have thought  
8 about this seven years ago when we started out  
9 before getting to this point.  
10 Now having gone through this, maybe the  
11 next generation of medicine will be able to do  
12 things a little more specific than we have.  
13 DR. FENDRICK: Last comment. One of  
14 the greatest surgeons that I know of in the U.S.,  
15 at least in this past generation was Maury Glesick  
16 of the Cleveland Clinic, who actually invented, or  
17 whatever term you use, use of the internal mammary  
18 artery for CABG, and was willing, after hundreds  
19 and hundreds and thousands of patients at the  
20 Cleveland Clinic, to do a randomized trial of CABG  
21 versus medical therapy, so it's not impossible.  
22 DR. LIEBERMAN: I am very willing to do  
23 that, and I have tried five times, and each time  
24 we've come up with other issues where the trial  
25 just hasn't gone. Now, we've got a number of

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1 individuals here, we all spoke over lunch and said  
2 let's do it, let's get together, we'll see what  
3 happens. I'm willing to randomize my patients. I  
4 do both procedures, I've got set criteria. I'm  
5 willing to take off my emotional hat because of  
6 what I believe is the right thing, to answer this  
7 scientific question that we haven't seen in seven  
8 years. And members of this panel, many of whom  
9 work with me, know that we tried this as  
10 desperately as possible. But the fact remains,  
11 there is still hundreds of thousands of patients  
12 that are coming to us demanding this treatment.  
13 DR. MCNEIL: I'd like to make sure that  
14 we don't get stuck on this one particular  
15 component. Do you have something additional to  
16 add?  
17 DR. EVANS: Just briefly. Avery Evans  
18 from the University of Virginia. Six years ago I  
19 tried to do that trial and I will just tell you,  
20 it is almost impossible to do. I would say at  
21 this point in time, it probably is impossible to  
22 do. Now other people can talk about that, it's  
23 unfortunate, it would be great if we could collect  
24 that data. I'll be frank with you. I think the  
25 only way we could possibly collect that data would

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1 be for this panel to say that vertebroplasty and  
2 kyphoplasty will no longer be paid for, and  
3 basically force patients to enroll in these  
4 trials. It is a grim fact that you're facing,  
5 because I can tell you that I have been there, I  
6 have tried for years to get patients to agree to  
7 be randomized to no therapy, and they won't do it,  
8 especially when they can walk down the street and  
9 find somebody who's willing to do it. I agree  
10 with you, we want to do it, tried to do it, and it  
11 is nearly impossible.

12 DR. ONDRA: I have a question that may  
13 help get us out of this randomized controlled  
14 corner. Have you looked at ways other than  
15 randomized controlled trials to get at Class I  
16 evidence? RCTs are not the only route to Class I  
17 evidence specifically, and it is not necessarily  
18 appropriate for all types of procedures. Is there  
19 any thought into looking at something other than  
20 an RCT that will give you Class I evidence?

21 DR. BURKE: Like what?

22 DR. ONDRA: In a large population  
23 specifically, it is not necessary to do a  
24 randomized control trial. At the University of  
25 Minnesota and University of California, San



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1 Francisco, there are statisticians that evaluate  
2 when you have a large enough number. There is a  
3 huge population of patients, this is a fairly  
4 common problem, and you could in all likelihood  
5 get to a large enough number that the absolute  
6 necessity and value of an RCT is no longer the  
7 only way to go about it.  
8 DR. BURKE: You still need people who  
9 aren't treated for control for unmeasured  
10 covariates, so even in a large population if  
11 you're not measuring the unmeasured covariates,  
12 you're still in a box.  
13 DR. ONDRA: But if you build in a study  
14 for this, because the point is, you can't get  
15 patients to do a randomized study, and I think  
16 that issue persists until you force people to do  
17 it.  
18 DR. MCNEIL: I see several people on  
19 the floor, but Dr. Jarvik, did you have a comment  
20 specifically related to this?  
21 DR. JARVIK: This is specifically  
22 related to the issue of the feasibility of doing a  
23 randomized controlled trial. As many of you know,  
24 Dave and I have been working on a randomized  
25 controlled trial for vertebroplasty here in this

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1 country and have had tremendous difficulty in  
2 recruiting patients for the trial for a variety of  
3 reasons. One of them is just the issue that Avery  
4 Evans raised, that it's paid for in this country,  
5 so people have an alternative to entering into the  
6 trial, to get something for which there isn't  
7 excellent evidence that it works. However, there  
8 are other countries where they have done this  
9 work. In fact in Australia, there is an ongoing  
10 controlled trial for vertebroplasty versus a  
11 controlled intervention and they have been much  
12 more successful than we have in recruiting  
13 patients. I think as of a month or so ago, they  
14 actually enrolled over a dozen patients in a  
15 relatively short period of time. And so, I think  
16 it may be potentially feasible to do, but maybe  
17 the climate has to change.  
18 DR. MCNEIL: I think I missed a hand.  
19 Dr. Fessler, did you have a comment?  
20 DR. R.G. FESSLER: It's specifically  
21 relevant to these issues, and that is, we've  
22 already said here repeated times that we lack the  
23 controlled studies and that we can't recruit  
24 patients. The other major issue that nobody said,  
25 these are tremendously expensive studies to do,

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1 and nobody is stepping up to the plate to pay for  
2 them. So given those variables, and I'll direct  
3 this to Dr. Belkoff or Dr. Marks, because you guys  
4 were the most vocal against the available data,  
5 what data can we accept if we can't do a  
6 controlled randomized study, and particularly with  
7 the questionable ethics of doing that with  
8 surgical patients anyway, what can we accept?  
9 DR. BELKOFF: Well --  
10 DR. MCNEIL: There were two people,  
11 before you answer that question, it looks like  
12 there were two colleagues that wanted to add  
13 something.  
14 DR. KALLMES: Well, I can say about  
15 this issue that everyone says we can't do it, and  
16 we had an NIH-funded trial, so there is money,  
17 \$2 million to do it, and I know I'm terribly  
18 underfunded, but let me give you the specifics.  
19 We have been up and running for a year at two  
20 sites, one a private practice site in Asheville,  
21 North Carolina, and one at Mayo Clinic. We have  
22 screened 500 patients, of which about 90 were  
23 eligible, of which three enrolled, and a three or  
24 four percent enrollment rate sounds bad.  
25 I'm optimistic. As the gentleman from

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1 Colorado said, he's their doctor, patients listen  
2 to their doctor. If the doctor comes to the  
3 patient in clinical practice and says we don't  
4 know, patients will enroll, as the study in  
5 Australia is learning. So it's not the  
6 appropriate time to throw up our hands and say it  
7 can't be done, we have funding to do it, but it  
8 depends on the clinical ethos of the  
9 investigators, which I think is substantially  
10 lacking in North America. It may happen overseas,  
11 but it may not happen in North America.  
12 DR. MCNEIL: Jim, did you have a  
13 question for the audience?  
14 DR. WEINSTEIN: Well, I would just echo  
15 Dave's point. I mean, I have been involved in a  
16 lot of randomized trials, we enrolled 2,500  
17 patients in 11 states, some of which are in this  
18 age group. I would argue that it's also very  
19 difficult and you need a lot of money.  
20 I guess my argument for the people  
21 presenting, though, even Dr. Avery, who had  
22 70-some patients, had 89 that he didn't collect  
23 any data on, and that's my question. Why aren't  
24 we collecting data on those patients who didn't  
25 have the procedure? You have hundreds and maybe

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1 thousands of them who would serve as some sort of  
2 control. I see no reason not to be collecting  
3 data on those patients. That is not an onerous  
4 task and I'm sure the money that the companies are  
5 paying would cover that.

6 DR. MCNEIL: Let's see now, we have a  
7 whole lot of people standing, and I'm trying to  
8 figure out what question they're answering.

9 DR. R.G. FESSLER: I'm still interested  
10 in Dr. Marks and Dr. Belkoff answering my  
11 question.

12 DR. GARFIN: I'm Steve Garfin from San  
13 Diego. I tried to develop a randomized controlled  
14 trial for kyphoplasty when it first started, at 25  
15 centers, probably 20 academic and five community  
16 practice. They were all my friends, they were all  
17 committed to it. Nobody else in town did  
18 kyphoplasty but those people. I spent a year and  
19 a half developing the protocol which you saw  
20 today, which we enrolled after two years 40  
21 patients. Halfway into the nonoperative arm,  
22 halfway into the procedure arm, there wasn't  
23 enough. The control group was to be nonoperative  
24 care, which included adding Fosamax or Actonel,  
25 giving them pain medication, controlled bed rest,

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1 physical therapy. So we couldn't do that, so what  
2 we settled on, because we couldn't get patients to  
3 enroll -- I mean, after two-and-a-half years we  
4 had 50 patients at 25 sites. So we settled on  
5 this prospective arm, set it up, so the next group  
6 of doctors who started using kyphoplasty had to  
7 agree to get involved in this study, which was how  
8 that second group occurred, because there was no  
9 way to enroll patients in the first group. Now  
10 everybody is coming in on antirestoratives, now  
11 everybody is coming in already with some kind of  
12 treatment, and now everybody is coming in having  
13 read all this information on the web which says it  
14 works, and in fact it appears to work, I think the  
15 data you have heard today says that. I don't even  
16 know what the control arm would be in today's  
17 world, because everybody gets osteoporosis,  
18 whether they're 40, 45, 60, everybody's on Actonel  
19 or Fosamax, so the control arm is pretty much  
20 gone. So, I don't know how to do randomized  
21 trials so that's why, again, we set up this  
22 prospective arm which was the best I thought we  
23 could do to get some science looking  
24 prospectively.  
25 DR. MCNEIL: Other comments? Is that

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1 on the same issue?  
2 DR. MARKS: Michael Marks, Norwalk,  
3 Connecticut. Maybe my practice is a little bit  
4 different in Fairfield County, but part of it also  
5 is that the average age of my patients is 80 years  
6 old. And to talk to some of these people and talk  
7 to them about the fact that we're going to  
8 randomize you to whether you're going to get a  
9 treatment or not treatment, in this day and age  
10 where there have been more than enough of these  
11 procedures done where these people know about the  
12 outcomes. I know it's not gold, but a month ago I  
13 had a woman come in to me saying she had had pain  
14 for a month, I'm not getting any better, I'm in my  
15 80s, I don't know how many more summers I have to  
16 play golf, I don't want to wait any longer. So  
17 that would be somebody who would not have opted  
18 into the study, and just getting these people in  
19 is a very difficult aspect of this, and I know,  
20 Dr. Fendrick, you're shaking your head, but that's  
21 the reality of being in a community-based  
22 practice.  
23 DR. FENDRICK: I need to quote Yogi  
24 Berra. Lumbar reduction surgery, I'm hearing it  
25 all over again. We were here sitting in this room

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1 in a different format basically talking about how  
2 every one of the people that came to present to us  
3 after taking out a defective lung, that patients  
4 were playing golf and the patients were living  
5 these happy lives. And it took the courage and  
6 integrity of the clinical community to say, we  
7 need to find out whether this intervention  
8 actually helps patients. Our first cut showed  
9 that it was actually killing certain patients more  
10 than helping them. The trial in Denver in fact  
11 showed that this intervention that was taking off  
12 at similar rates as this is, with the same level  
13 of scientists of dedication and compassion, it  
14 turns out that all those people who came in with  
15 the same amount of zeal looked at that result from  
16 randomized trial and shook their heads saying, I'm  
17 really glad we did this study and I'm pretty  
18 surprised with what we found. I'm not discounting  
19 anything you're saying. I'm just saying it's one  
20 of those things that those of us who are shallow  
21 like me, who look across conditions, we've seen  
22 this so many times where someone has to take the  
23 point of view that this may not be right.  
24 DR. MARKS: But I think the other issue  
25 that I hope you heard today is that there are



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1 700,000 vertebral compression fractures out there.  
2 I think what you've heard from at least the  
3 community-based doctors is that we're probably  
4 operating on ten percent of the fractures that we  
5 see, so a lot of them are getting better, there  
6 are those that just are not getting better, and we  
7 have an alternative treatment for them.  
8 DR. FENDRICK: A great majority of our  
9 80-year-old patients don't have their tonsils  
10 because surgeons believed that was helpful as  
11 well.  
12 DR. MCNEIL: You had asked Dr. Belkoff  
13 a question, is that correct?  
14 DR. R.G. FESSLER: Yes.  
15 DR. MCNEIL: He now has the opportunity  
16 to answer.  
17 DR. BELKOFF: I forgot what the  
18 question was, but I will answer anyway.  
19 Basically, it's not what you guys want, it's what  
20 the standard is or how high the bar is set. I  
21 personally think that a randomized controlled  
22 study would be a nice thing to see. Barring that,  
23 I understand the complexities of that, I know  
24 there's a study ongoing, but oddly enough in  
25 France, where Dr. Germon tried to do a prospective

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1 study, the problem he had was just the opposite,  
2 he couldn't get his primary care physicians to  
3 refer patients to him because they all thought it  
4 was voodoo and they wouldn't give him the patients  
5 to put the cement in to see if it had any  
6 palliative effect, and to this day they are still  
7 not reimbursed in France for doing  
8 vertebroplasties. So it's just the opposite.  
9 Maybe we can get together with France and ship  
10 people across the ocean.  
11 But the next level, I think, and I'm  
12 not, although I will be soon I think, an  
13 epidemiologist, I don't know what the best  
14 controlled study would be. There was one option  
15 put out a while ago where you would allow patients  
16 to enroll, they would be assigned randomly to a  
17 conservative treatment group, but after a certain  
18 period of time they could cross over. I think,  
19 Dr. Weiner, you would be most qualified to answer  
20 this question as to what sort of bias that might  
21 introduce, but that would I think, as I see it,  
22 the compromise for evidence in saying that you  
23 give them a chance to try conservative therapy for  
24 a period of time. If the lady wants to golf this  
25 summer and things aren't working out very well,

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1 that she can cross over, she can hold that hope  
2 out, and maybe we will at least get two or three  
3 weeks worth of data, or six weeks, and see if the  
4 fracture will heal on its own, and it at least  
5 gets us where the Australian study was. That's  
6 all I can offer, I don't know. It may be like a  
7 bottle of elixir.  
8 DR. FENDRICK: Will it make my hair  
9 grow back?  
10 DR. BELKOFF: It will cure lumbago,  
11 sciatica, bad breath and constipation.  
12 (Laughter.)  
13 DR. MCNEIL: So Dr. Jarvik.  
14 DR. JARVIK: Yeah, briefly, that's how  
15 we conducted our trial, had a relatively short  
16 crossover time point of four weeks, so that people  
17 are actually guaranteed to get the procedure  
18 within a relatively short time period. And in  
19 some sense, that's the weakest point analytically  
20 of the study, but it also is a strength as far as  
21 recruiting and that is what everyone is going to  
22 get potentially with both procedures.  
23 DR. MCNEIL: Dr. Sullivan, did you want  
24 to add to that? I want to be sure that you all  
25 aren't going to run out of time in terms of saying

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1 important things to us, and that we've all asked  
2 you all the questions that we want. What question  
3 were you answering?

4 DR. MCKIERNAN: Just a comment on

5 Dr. Fendrick's position.

6 DR. MCNEIL: Okay. So maybe we can  
7 make a quick comment, and then open it up for new  
8 sets of questions, and we will do this for about  
9 five minutes.

10 DR. MCKIERNAN: I think your concern is  
11 spot on, and my concern is that we reconvene in  
12 ten years and have the same bad data to go over  
13 again, we will have learned nothing. So I do  
14 think there is an opportunity that the correctly  
15 designed study can be done. For us it's money,  
16 but we're in a unique setting where everyone comes  
17 to see us, and my concern is that we don't need  
18 more data, we need better data. If we keep  
19 designing studies the way that we have been and  
20 are careless with patient selection, clearly with  
21 those measurements, outcomes, et cetera, we will  
22 be no smarter.

23 DR. MCGRAW: Kevin McGraw, Columbus,  
24 Ohio. I was part of two randomized placebo  
25 controlled trials, one was at Carolina Accutron,

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1 and I was also part of Dr. Kallmes' NIH-funded  
2 trial. We have a very busy vertebroplasty  
3 practice in Columbus, Ohio where we do 500  
4 procedures a year. To try to enroll patients in  
5 those studies, I interviewed 125 patients. They  
6 knew going in that they could cross over if they  
7 were randomized to the control arm of the study.  
8 Not a single patient wanted to be in pain for  
9 another four weeks before crossover. It's  
10 exceedingly difficult to enroll patients into a  
11 trial of that nature.

12 DR. MCNEIL: Thank you very much.

13 DR. BIAN: I'm John Bian from UAB, I'm  
14 an assistant professor of preventive medicine, and  
15 trained as an economist, and I just wanted to make  
16 a brief comment about are there any other ways  
17 other than RCT to assess the outcomes of the  
18 procedure. I firmly believe that RCT is the  
19 standard, but one step back, I think there are  
20 potential other methodologies, but each one with  
21 some limitation. Someone proposed to do an intent  
22 analysis, but the problem is there will be  
23 uncontrolled confounder. Someone could do that,  
24 but it's extremely difficult to define. It's a  
25 very nice technique in theory, but I found only

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1 one article published in 1994, which one of the  
2 authors studied the outcome of (inaudible). For  
3 instance, there are other means which have other  
4 names, the epidemiologists call it case crossover  
5 analysis. In economics we call it individual  
6 (inaudible). So the one catch of this type  
7 analysis is you need to have repeated  
8 measurements, repeated treatment on the same  
9 individual over time, and you also like to observe  
10 variation in outcomes over time. I don't think  
11 this type of data is available at the present time  
12 because we're trying to do that technique, but we  
13 don't have enough patients who have multiple  
14 treatments or outcomes.  
15 DR. MCNEIL: Thank you very much.  
16 DR. LIEBERMAN: This is Lieberman, from  
17 Cleveland Clinic. Two quick comments just in  
18 response to Dr. Ondra and in support of my initial  
19 comments to Dr. Fendrick.  
20 Is there something other than a  
21 randomized controlled trial? Well, this is right  
22 out of Spine, of which Jim Weinstein, the editor,  
23 is sitting right there. Is there a continued role  
24 of prospective observational studies in spine  
25 research, and the answer to this, or from this

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1 editorial is yes, there are, if they are  
2 controlled properly and designed properly. And  
3 you've heard from my crowd, from Dr. Evans, Dr.  
4 Mathis, there's a number of names who have given  
5 us these prospective controlled trials with good  
6 information that shows objective outcome measures.  
7 Now, the second point is, why have we  
8 completely discounted the outcome studies from the  
9 drug trials that show that these patients with  
10 osteoporotic compression fractures get worse over  
11 time, that show that mortality is bad over time?  
12 Can't we somehow take that information and marry  
13 it to the information we have today and show,  
14 look, my SF-36s show us in two years these guys  
15 are doing better, they're much better than their  
16 baseline when they got there, and when you compare  
17 that to the historical controls, we do have  
18 evidence that this procedure, these techniques do  
19 help our patients. Thank you.  
20 DR. HIRSCH: Josh Hirsch from Mass  
21 General. I wanted to address each of these  
22 questions, particularly Dr. Weinstein's about  
23 radiologists performing these procedures, but I  
24 held my tongue. This I think is really important  
25 to address because we wanted to do this trial.

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1 This isn't lip service, I'm not on Jerry Jarvik's  
2 committee, and I believe in this stuff, I really  
3 do. I was on the active (inaudible) we don't do  
4 sham trials, through my IRB, and I was humiliated.  
5 I would like to make an anecdotal  
6 remark, which is that at 105, which is the oldest  
7 of my patients, six weeks is a long time. And I  
8 would also like to make the further observation,  
9 having stated that I believe in these studies and  
10 I also believe in these procedures, which is an  
11 obvious bias, but the point I tried to make  
12 before, conservative therapy does have its own  
13 risks and we shouldn't discount those risks. Two  
14 to four weeks of additional narcotics, of lying in  
15 bed, of enhanced hormones, shouldn't in my opinion  
16 be expected.  
17 The final point I would like to make,  
18 though, I know it was only in abstract form, and  
19 I've offered to help them write it, we developed a  
20 very nice prospective study out of Stanford which  
21 I don't think I could do today. It was  
22 referenced, but not referenced as clearly in my  
23 opinion as Ed Kallmes's five patients, for the  
24 ability to do a sham trial. And I think it should  
25 be given at least equal weight to that because I



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1 think it was a legitimate effort. Thank you.  
2 DR. MCNEIL: Dr. Burke.  
3 DR. BURKE: I think that pain is a very  
4 problematic outcome, it requires proper  
5 instruments, it requires that the instrument is  
6 administered objectively, which is important in  
7 its own right. I think back pain is very  
8 difficult and requires especially rigorous  
9 settings, and I think back pain more than any  
10 other problems has a host of issues that we've  
11 seen over the years, which demand extremely  
12 rigorous studies. I think there are some general  
13 problems with this data and I don't see how they  
14 are going to be overcome with these prospective or  
15 retrospective studies.  
16 I agree with the Blue Cross assessment  
17 and believe there is questions to be made. I  
18 think there are powerful placebo effects related  
19 to the procedures. I think there may be patient  
20 selection biases at work here. I think the use of  
21 validated pain assessment instruments are  
22 required. I think that the issue of unblinded  
23 administering of the pain instrument is a critical  
24 problem. I think the natural history of back pain  
25 is not addressed. How are they controlling for

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1 the medical management of these patients through  
2 this process? I think the issue of the Hawthorne  
3 effect, that just by doing something to these  
4 patients, by paying attention to them, you get a  
5 benefit, that's well known. I think there is  
6 confounding outcome covariates and I think these  
7 issues have not been addressed sufficiently to my  
8 mind.  
9 I think there are a number of  
10 unanswered questions. What is the best comparison  
11 group? Which patients will benefit from the  
12 treatment? What are the best instruments used to  
13 measure the effects? Are we looking at systematic  
14 pain management as a comparison or are we looking  
15 at the ad hoc pain management? And then finally,  
16 what is the appropriate time interval for the  
17 outcome measurement.  
18 DR. SULLIVAN: I have a comment and a  
19 question. So, the comment on alternative study  
20 designs, there's been suggested a couple. I would  
21 like to point out that in the late '90s, there was  
22 a paper published in JAMA using instrumental  
23 variable technique to investigate pulmonary artery  
24 catheterization and it was a very important study,  
25 and showed the use of an alternative methodology

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1 rather than the randomized control trial. The  
2 problem, though, as mentioned, is you need people  
3 who didn't receive the technology for comparison  
4 purposes.  
5 So, my question is, we're basically  
6 evaluating a lot of data here that are essentially  
7 case series, they're not trials, and what I need  
8 to understand is, what happens to the patients who  
9 drop out of the case series? Dr. Lieberman just  
10 suggested that we study his two-year SF-36 data.  
11 There's only 48 patients out of 329 at two years,  
12 that's a 15 percent follow-up. I would like to  
13 know if anyone can characterize for me the kinds  
14 of patients that aren't followed up and don't have  
15 SF-36s at the one-year follow-up, which according  
16 to your case series was only 30 percent of cases.  
17 So, can someone who has published these case  
18 series just help me understand the people who drop  
19 out who you don't have measurements on, tell me  
20 about them clinically.  
21 DR. LIEBERMAN: One of the things we  
22 have to be careful about when we start looking at  
23 those percentage numbers, when we said that there  
24 were 48 patients at two-year follow-up with 72  
25 percent of them, that meant that we had 55 full

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1 patients with two-year follow-up, on which I only  
2 had full data on that 48, that's where that number  
3 72 came from. Now the two-year follow-up, sure,  
4 is only a small portion of that, and those are  
5 patients I did way back in 1999 and 2000 and 2001  
6 that we have continued to follow up as long as we  
7 possibly could.

8 Now we have lost a number of patients  
9 through attrition, some die, some move, some just  
10 don't bother coming back, but we have tried to  
11 follow as best we can. So those groups were  
12 divided down in that intact population according  
13 to those yearly breakdowns that we had there, so  
14 it's not that it was only 15 percent follow-up at  
15 two years, we had 55 patients or whatever that  
16 number would be to make that 72 percent or  
17 whatever it was that we had.

18 DR. SULLIVAN: I'm not sure you  
19 answered my question, to help clinically  
20 characterize the patients who you haven't followed  
21 up on for all those reasons, but in your graph  
22 here it's 48 patients that you have an SF-36  
23 measure on when you say minimum of 24 months of  
24 follow-up.

25 DR. LIEBERMAN: Right. And there's a

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1 percentage number beside that, I don't have it in  
2 front of me, but 70 percent right at the very top  
3 of that graph.

4 DR. SULLIVAN: There is no percentage  
5 there other than the one I calculated.

6 DR. LIEBERMAN: I don't know why that's  
7 not up there, but it should be. Of the 48 that we  
8 had, that ended up being 72 or 73 percent of the  
9 total that we had for two-year follow-up.

10 DR. SULLIVAN: Okay. Let's assume it  
11 was 55. So even 55 out of 329 is very few  
12 patients.

13 DR. LIEBERMAN: But those are the  
14 patients that we did very early on, those are the  
15 ones that I managed to follow through that still  
16 kept coming back.

17 DR. SULLIVAN: So back to my main  
18 point, can you tell me about those patients, were  
19 they sicker, were they healthier, did they not  
20 receive benefit from the treatment and decide that  
21 they weren't going to come back to you to follow  
22 up or participate in your study because they were  
23 off at a naturopathic healer or something?

24 DR. LIEBERMAN: We tried to follow  
25 those patients up beyond one year as much as we

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1 possibly can. When they don't come back, I can't  
2 tell you why they don't come back. We tried to  
3 chase them up, and these are the best numbers that  
4 we could possibly do short of physically moving  
5 into each and every one of these patients' homes  
6 and seeing how they're doing. We tried as best  
7 we can and those are the numbers that I have, so I  
8 can't comment on what happened to them after or  
9 why they didn't come back.

10 DR. FENDRICK: But if they came back  
11 for a visit at one year and said they were less  
12 satisfied, there is something we would be able to  
13 see there.

14 DR. LIEBERMAN: Well, that's what we've  
15 got and that's why we've broken it down, and  
16 that's the basis of the paper that we submitted to  
17 Osteoporosis International. We've broken it down  
18 based as the whole group, the two-year group, the  
19 one-year group, and the six-month group, to look  
20 at that. So with each one of those groups, the  
21 numbers go up in terms of the follow-up and you  
22 can make some conclusions. In each one of those  
23 groups, we showed statistically significant  
24 sustained improvements in their SF-36 numbers  
25 across the board.

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1 DR. BURKE: You know, in cancer, I  
2 mean, you know, the follow-up that we look at, the  
3 people who drop out invariably have a worse  
4 prognosis, that's almost always found in cancer.  
5 That's in cancer, but I think in other fields, I  
6 think they have similar findings and many times  
7 the people who drop out are the ones with worse  
8 prognoses.  
9 DR. R.G. FESSLER: My personal findings  
10 are very different than that, because I didn't  
11 follow a vertebroplasty group, but a lumbar fusion  
12 group for two years and at two years many of our  
13 patients weren't coming back to clinic. So we  
14 called them and we hounded them, and when we got  
15 hold of them what they said was no, I'm not coming  
16 back, I'm fine, leave me alone.  
17 DR. ONDRA: I think it is a very  
18 different issue in cancer and other outcomes, and  
19 the follow-up or lack of it may be for different  
20 issues.  
21 DR. LIEBERMAN: If I could just make  
22 one comment, I'd just like to clarify something  
23 with Dr. Burke. Vertebral compression fracture  
24 pain is very, very different than the degenerative  
25 low back pain, we're dealing with two different

00200

1 animals here, so I'm not sure that I'm comfortable  
2 with that generalization and lumping all of this  
3 as back pain.

4 DR. BURKE: Well, I'll just answer.  
5 It's a slippery character and we have to be aware  
6 of that.

7 DR. LIEBERMAN: Granted, but they are  
8 two different patient populations and groups and  
9 etiologies of pain.

10 DR. RESNICK: Just a comment, if I may,  
11 actually addressed to Dr. Burke. We're not curing  
12 cancer here, we're not going to improve these  
13 patient lives for the rest of it, they still have  
14 osteoporosis, they're still 80-some years old,  
15 they're still going to have future problems. What  
16 we're doing here is providing immediate pain  
17 relief that appears to be lasting, which at two or  
18 three years out may have actually no benefit,  
19 where if you measure out two or three years out,  
20 but there is still an intrinsic benefit in that  
21 pain relief that you get for the avoiding that six  
22 weeks of bed rest or the morbidity associated with  
23 the initial fracture pain.

24 DR. BURKE: I mean, it may be that it  
25 isn't a durable effect, maybe it is. I wish I



00201

1 knew by the evidence.  
2 DR. GARFIN: Steve Garfin, from  
3 San Diego. I presented two-year data on a  
4 multicenter trial and to answer your question, we  
5 know the numbers. We entered 155, I reported on  
6 100. We know what happened to those 55, I have  
7 the breakdown. I don't have it right down here,  
8 but a certain percentage of them died, and the  
9 average age was 77 that we're dealing with, from  
10 unrelated causes reported on the two-year data.  
11 Some, like Izzie said, just felt good and didn't  
12 want to come back. Some didn't have a ride. Some  
13 developed other medical problems and were  
14 hospitalized elsewhere and just couldn't come  
15 back. Of the data points we had, which I didn't  
16 report because I didn't want to confound or deal  
17 with too many statistical variables, they followed  
18 the same standpoints, they followed the same  
19 parameters, they did all the same tests until they  
20 dropped out. They looked the same,  
21 demographically they looked the same datawise, but  
22 I didn't report them. But there were 55 that  
23 dropped out and we know what happened to all but  
24 five that we just couldn't track.  
25 DR. MCNEIL: Go ahead.

00202

1 DR. ONDRA: I have a different question  
2 and that's to talk about morbidity. Do you have  
3 any data on the role of morbidity and not having  
4 good control, the relative morbidity of  
5 nonsurgical treatment versus surgical treatment of  
6 those populations?  
7 DR. LIEBERMAN: Are you looking at me?  
8 DR. ONDRA: Any of you.  
9 DR. DOHM: No, we don't have, and  
10 that's the point. We have all this other data  
11 that helps us with the impression that we are  
12 making a difference in these patients' lives.  
13 DR. MCNEIL: Let's see. Jonathan, you  
14 had a question, or comment?  
15 DR. WEINER: Yeah, building on  
16 short-term, long-term, the best that we've got out  
17 there, and I think Blue Cross identified it, were  
18 the comparative, not controlled groups, and one  
19 was in German and my German is not very good, but  
20 as it turns out, one was Australian and two were  
21 German, and I found another one in the Hopkins  
22 library coming out next month from Vienna, some of  
23 you may already know about that, Dr. Gross, and  
24 they're all either European or Australian. How  
25 are they doing that and we're not? Is the

00203

1 difference that we're not paying for it outside of  
2 this context, or are they being tougher on their  
3 patients? Granted, these aren't perfect studies.  
4 The next one also is similar to the German and  
5 Australian, it's a comparison, prospective, two  
6 years, solid disability and pain measures, and  
7 again define that by the short-term.  
8 DR. MCNEIL: Dr. Kallmes.  
9 DR. KALLMES: I can address that. I've  
10 spoken to the investigators in Australia. I think  
11 what Dr. McGraw is here saying, Dr. Evans and Dr.  
12 Hirsch, they are the wrong people to be talking  
13 to. They are probably the worst people to be  
14 talking to, because they get the patient referred  
15 to them after seeing their internist, their  
16 endocrinologist, their rheumatologist. They come  
17 with this preexisting bias built in by the  
18 referring physician. The studies that are  
19 succeeding overseas are PIs, not a radiologist,  
20 but in fact endocrinologists or rheumatologists.  
21 So that's the reason, I think it's the physician.  
22 Again, patients listen to their doctors, but we  
23 are the wrong doctors to do that. You've got to  
24 reach out to the primary care people who will not  
25 instill bias.

00204

1 DR. WEINER: Do they have payers  
2 involved, do they mandate it?

3 DR. KALLMES: Australia has stopped  
4 paying for vertebroplasty.

5 DR. WEINER: How about Germany and  
6 Austria.

7 DR. DOHM: Just to follow up on Dr.

8 Kallmes, what I'm seeing in my practice and again,  
9 do I have the statistics, no, but what I see is  
10 I'm an orthopedic surgeon in the era of managed  
11 care and we have a lot of managed Medicare. These  
12 patients need a referral to come to me, they are  
13 not just picking up the phone to come see me. And  
14 so by the time they get to see me, most patients  
15 have had, because of the time wait to get to see  
16 me, four weeks, six weeks, time to get the MRI and  
17 all the other stuff. It is rare for me to get a  
18 patient in the operating room to consider doing a  
19 kyphoplasty before six weeks. The simple fact is,  
20 there is just too much delay in the system. And  
21 if I have a patient who comes to see me who had  
22 pain and then comes back, and I've actually had it  
23 happen once in the four years, I cancel the  
24 procedure, because that was somebody who had a  
25 minimal depression fracture, it was five percent,

00205

1 they come in to see me, there wasn't a lot of  
2 deformity associated with it, the pain went away,  
3 so I didn't do the procedure. But almost every  
4 other patient, by the time it's six weeks, like  
5 the 80-year-old patient, or this past week, and I  
6 know it's another anecdote, the 90-year-old woman  
7 who has been having pain for six weeks, told me  
8 she needed to have the procedure done because she  
9 needed to take care of her handicapped 82-year-  
10 old.  
11 DR. FENDRICK: We hear you loud and  
12 clear, but if you were just collecting the data on  
13 those people that were waiting to come into your  
14 operating room, we would be much more comfortable.  
15 Not even, no study design, just checking the raw  
16 descriptive data on six weeks of natural history  
17 would make a lot of us feel much better. Since I  
18 don't do trials in this area, I heard at least an  
19 inference that the companies that are supporting  
20 other trials, given that this piece of a case  
21 report form or data collection would be marginal  
22 over the larger studies that all of you are doing,  
23 hearing this makes me feel even more frustrated,  
24 knowing that you had the opportunity to collect  
25 six weeks entry data on these patients and haven't

00206

1 done it. Now I'm not speaking to you directly,  
2 I'm looking to the community. You have all had  
3 that opportunity, whether the wait list in western  
4 Colorado is two weeks and in Cleveland it's four  
5 weeks, but the people who are not coming in that  
6 day, you could be collecting that data to the  
7 point that Jerry Jarvik's study at four weeks and  
8 six weeks, you might even have some really  
9 important information on what his control group  
10 might look like.

11 DR. MARKS: But I guess to me, and  
12 maybe somebody mentioned it before, the main issue  
13 is, and I think Izzie was saying before, a lot of  
14 us are more than happy to do it. I guess the  
15 question is, we need to put together an organized  
16 set of questions so that we're all on a large  
17 scale asking the same thing and gathering the same  
18 data, and then having a repository where we can  
19 basically submit that. Because I can tell you as  
20 a private practitioner, I don't have the financial  
21 resources nor the time to go ahead and do those  
22 things.

23 DR. FENDRICK: I've seen the same thing  
24 in cardiology, pulmonology, gastroenterology. I  
25 would recommend going to a very fancy resort with

00207

1 12 of your colleagues and set up one of these  
2 registries that collect these data that we're  
3 talking about. It's not that hard to do and  
4 there's lots of examples in other areas that it's  
5 been pulled off.  
6 DR. R.G. FESSLER: What about the data  
7 that was presented today? On the one hand we're  
8 saying you guys ought to collect it, and on the  
9 other hand we're seeing it presented right in  
10 front of us and we're saying it's not good enough.  
11 DR. GARFIN: Steve Garfin, on  
12 Dr. Kallmes's comment. When we were failing in  
13 the prospective controlled RCT trial to get  
14 patients enrolled, we did go to three or four  
15 internist or endocrinologist or osteoporosis  
16 centers to get them to enroll the patients for us  
17 to avoid the surgeon's arm, and they couldn't do  
18 it either. This was back in '99. Because the  
19 patients went across the street to get  
20 vertebroplasty, we just couldn't get them in, even  
21 at the primary level.  
22 DR. MCNEIL: All right. We will have  
23 just a few more questions for the audience. Did  
24 you want to add something?  
25 DR. DOHM: I just would like to make

00208

1 one comment with respect to the idea of  
2 registries, et cetera. I've had some involvement  
3 with that, and maybe Dr. Weinstein could comment  
4 as well, but for 30 years our American Academy of  
5 Orthopedic Surgeons has really looked at trying to  
6 have a joint registry, it seems pretty simple and  
7 it's analogous to doing this with the spine but  
8 it's a lot more difficult. There are so many  
9 personal issues that are at hand, and the  
10 difficulty now is we just met in Washington, D.C.  
11 for our academy in February. We worked three  
12 years on putting together the American Joint  
13 Replacement Registry, because every other big  
14 nation already has a registry for joint  
15 replacement and we thought it would be fairly  
16 simple to do. We have a contract with Eclipsis  
17 and Sun Clinical, they could come up with the  
18 software to sort of back us up and help us. We  
19 already have 13 hospitals that are IRB-approved  
20 across the country, University of Wisconsin, and  
21 something that simple, we can't do it. I think  
22 we're getting closer to the point of being able  
23 to, but it's just extremely difficult.  
24 DR. MCNEIL: I want to ask one thing,  
25 and the question is as follows: It looks as if



00209

1   however we criticize the design of the studies, we  
2   have some follow-up data to two years, and it's  
3   not a complete follow-up at two years or whatever  
4   the time frame is, so my question is the  
5   following: How can you be sure or what confidence  
6   can you give me that your last follow-up period,  
7   there isn't an increased incidence of adjacent  
8   fractures in the group treating these procedures?  
9   That was raised as one of the classical long-term  
10   complications, and I fail to see how you've  
11   convinced me that there isn't. I'm looking for  
12   data to the contrary, I don't want just thoughts.  
13   DR. LIEBERMAN: Izzie Lieberman,  
14   Cleveland Clinic. We published in October of 2004  
15   the follow-up that I referred to in my talk  
16   looking at 115 patients with 225 kyphoplasties,  
17   and we found an 11 percent incidence of remote and  
18   adjacent level fractures within the osteoporotic  
19   group. Within the secondary osteoporotic group,  
20   they had a 45 percent rate.  
21   DR. MCNEIL: And what time period was  
22   that?  
23   DR. LIEBERMAN: That was at 12 months  
24   minimum in that group of patients.  
25   DR. MCNEIL: So, do you have anything

00210

1 out further than that?

2 DR. LIEBERMAN: Further, we haven't  
3 fully analyzed that, and that's part of the  
4 process that we're going through right now with  
5 that same group of patients.

6 DR. MCNEIL: So the original question,  
7 then, is what percentage of the total patients was  
8 that?

9 DR. LIEBERMAN: At that point in time  
10 that was 115 out of I think it was 175 patients  
11 that I had treated at that point. What we had  
12 done is excluded the myeloma patients out of that  
13 group, so it was the whole group that we had  
14 treated from I think it was April '99 to the 2001,  
15 actually I think it was 2002, in that span, we  
16 treated over 200 patients, and it was 11.25  
17 percent up to 12 months, remote and adjacent, and  
18 about half of those were adjacent and half were  
19 remote at other levels.

20 DR. MARKS: Michael Marks, Norwalk,  
21 Connecticut. I actually looked at my patients  
22 during 2004 and it was in the fall because of the  
23 article in Spine by Freiberg which was quoted to  
24 you earlier. I looked at my first hundred  
25 patients who had then been out two years and I

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1 found similarly that it was roughly 12 percent  
2 refracture. Actually it was 14 percent refracture  
3 rate for all comers and when I substituted out the  
4 secondary osteoporotics, my number turned out to  
5 be about 8 or 9 percent for those who had primary  
6 osteoporosis and 32 percent for these who had  
7 secondary osteoporosis.

8 DR. MCNEIL: Okay, do you have a  
9 number?

10 DR. CHER: Daniel Cher from Kyphon. As  
11 you recall from the presentation I gave, the two  
12 prospective controlled studies from Germany both  
13 addressed this issue. The first study showed a  
14 decrease in subsequent fracture rate with balloon  
15 kyphoplasty as opposed to nonsurgical treatment  
16 after six months.

17 DR. MCNEIL: Did it go out any further,  
18 12 or 24 months?

19 DR. CHER: We are aware of one-year  
20 data which I believe have been submitted to a U.S.  
21 journal, I think they have been submitted, and  
22 they do show a statistically significant reduction  
23 in subsequent fracture rate at one year.

24 DR. MCNEIL: What's the raw number? I  
25 don't think I can relate to a reduction unless I

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1 know what the control group is.  
2 DR. CHER: It's actually in my  
3 presentation, I cannot recall. New occurred in 7  
4 of 19 patients treated with balloon kyphoplasty.  
5 DR. MCNEIL: That's at 12 months?  
6 DR. CHER: That's the six-month data.  
7 And 11 of 17, if I recall the numbers, were 37  
8 percent versus 65 percent. The other study, also  
9 from a German investigator that was published just  
10 last month, showed at 12 months, 5 percent versus  
11 30 percent, and again, this is at six months.  
12 This one-year data is also available.  
13 Individually, both of these studies,  
14 the six-month data are not statistically  
15 significant reductions; however, when you put them  
16 together, they are statistically significant, and  
17 it's my understanding that the one-year data from  
18 the first study which has recently been submitted  
19 does by itself show statistically significant  
20 reduction in the rate of subsequent fractures  
21 attributable to balloon kyphoplasty, so there is  
22 actually data from concordant, granted not  
23 randomized, but concordant studies.  
24 DR. MCNEIL: Thank you very much.  
25 DR. FENDRICK: A brief final point is,

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1 not to sound like a broken MP-3 player since my  
2 kids don't know what a record is, but looking at  
3 the effective size that you have all presented in  
4 your nonrandomized controlled trials and the  
5 information that you find, I don't have my  
6 calculator here in front of me, but I will tell  
7 you that a randomized trial to show pain reduction  
8 would not have to be very large, and I think  
9 that's another thing, and I'll probably hear from  
10 the NIH-funded trials again, but I'm actually  
11 thinking that this, if you're plugging away at ten  
12 patients a year, I think you're going to be able  
13 to get the numbers you need to at least reach some  
14 of those primary end points much sooner than a lot  
15 of you people who feel that these studies cannot  
16 be done will actually happen.  
17 DR. CHER: I agree that the study size  
18 not does not have to be large. I just wanted to  
19 note that the (inaudible) for subsequent fractures  
20 is roughly 0.3, so that's a 70 percent decrease  
21 from these two studies.  
22 DR. MCNEIL: Yes, Josh.  
23 DR. HIRSCH: Josh Hirsch, Mass General.  
24 I just want to make a quick point. I think Dr.  
25 Kallmes is right (inaudible) the committee, which

00214

1 is far more expert on studies, I submit to you  
2 that you've told us that the studies are being  
3 done abroad and that they're succeeding. So why  
4 contemplate such a destructive change in how we're  
5 helping people now when studies will be available  
6 in I imagine a short period of time.  
7 DR. FENDRICK: If the Australian study  
8 is negative, will you be willing to stop doing it?  
9 DR. HIRSCH: I think I would submit to  
10 randomized controlled data if that went the wrong  
11 way, I have to be honest about that, and I have I  
12 hope stated my bias clearly. I accept it. I  
13 really believe in these procedures and for this  
14 reason I have trained many people to do these  
15 procedures, but I think I'm an honest  
16 practitioner, and if randomized controlled data  
17 comes against what I think, then I have to accept  
18 it as such.  
19 DR. BURKE: But you know, we've seen  
20 that in cardiology, TPA (inaudible) worked and the  
21 American cardiologists didn't agree to that, and  
22 those are randomized trials in Europe, so it's not  
23 always like that.  
24 DR. HIRSCH: The other half of my life  
25 is in cerebrovasculature and I've watched

00215

1 controlled studies or studies of that ilk  
2 absolutely change practice in the United States.  
3 Those surgeons, one of them spoke how they now  
4 perform far more minimally invasive procedures in  
5 surgery. I would like to think that the community  
6 would respect the results of it. I will say this.  
7 I believe (inaudible) CMS or Medicare reimburses  
8 for these procedures will be unruly and disruptive  
9 to the patient that we treat. I'm at an academic  
10 center, they don't have my salary published, but I  
11 don't think I'm making money in doing these  
12 procedures; in fact, it probably costs my  
13 department that I do these procedures instead of  
14 more lucrative procedures. I've stated my belief,  
15 thanks.

16 DR. MCNEIL: Thank you very much. All  
17 right. Let me just make sure there are no other  
18 additional questions from members of the panel to  
19 the audience.

20 DR. WEINSTEIN: How are those studies  
21 supported, the European studies, who funded them?  
22 How are they funded?

23 DR. KALLMES: The one in Australia was  
24 funded by the government.

25 DR. WEINSTEIN: And the German studies?

00216

1 DR. MCNEIL: Jonathan, do you have  
2 that?

3 DR. WEINER: By Kyphon Europe and the  
4 German government.

5 DR. MCNEIL: Other comments or  
6 questions? Did you have a question that you  
7 wanted to answer?

8 DR. TALMADGE: There were a couple  
9 questions that I wanted to comment on briefly. I  
10 would like to clarify with the panel that I  
11 believe that there is far more data on the  
12 outcomes of the natural history than is being  
13 appreciated right now. I point to a series of  
14 papers that have been published over the last ten  
15 years demonstrating how the osteoporotic condition  
16 impairs function and quality of life, and there's  
17 about ten papers that really are very powerful in  
18 terms of these outcomes.  
19 And then in addition, more recently  
20 there's been a prospective study that was done  
21 where they actually have all the patients who had  
22 acute fracture and they followed them for two  
23 years, and the outcome that was measured was  
24 SF-36. And in physical function, vitality, social  
25 function and one other domain, there was no change



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1 in the SF-36 scores in spine fracture patients for  
2 two years. There were some minimal changes in the  
3 other SF-36 domains but they did not in any way  
4 reach the case controls that were also part of  
5 that study, and they did not compare to the hip  
6 fracture patients which got better.  
7 In addition, there is a separate cohort  
8 from Sweden that is available on the web, it's not  
9 yet published, but it's an ongoing study that  
10 confirms these SF-36 results. So I think there is  
11 a substantial body of independent data that says  
12 that the management, the nonoperative management  
13 of these patients in the near term doesn't address  
14 their symptoms and in the long term creates a  
15 deformity that impairs function and quality of  
16 life. So, that was that comment.  
17 Also, I would just like to comment on  
18 some of these studies that have shown that  
19 treatments that were thought to work don't, and in  
20 particular I would like to mention Mosley, which  
21 was in the New England Journal of Medicine, it's  
22 the one that's referred to as the lavage study,  
23 the study of the arthroscopic lavage. And in that  
24 study, I'd just like to remind everybody that in  
25 that study, there was no benefit of the

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1 arthroscopic lavage itself or of the placebo  
2 treatment. So it wasn't that we saw a placebo  
3 effect, it was that we saw no effect.  
4 And if you look at the observational  
5 studies, unlike the kyphoplasty and  
6 vertebroplasty, the observational studies in fact  
7 were mixed, and there were many that showed no  
8 benefit and some that showed some benefit, but  
9 there were very few studies with objective  
10 outcomes, and the randomized study has to have  
11 objective outcomes. So I do think that's a very  
12 different situation than we have right now where  
13 we have profound immediate changes.  
14 And then I'd also like to just mention  
15 some unpublished data from the Women's Health  
16 Initiative, something that I have always  
17 suspected, which is, that study was performed in  
18 women who are 65 years of age, and all the  
19 observational studies were performed in women who  
20 were perimenopausal. They have now done a  
21 subanalysis and it will be published, showing that  
22 in the cohort in the first decade after menopause,  
23 that they have exactly the same outcomes as the  
24 observational studies, so when the patient  
25 populations were matched, the patients did in fact

00219

1 do just as well in the randomized study as they  
2 did in the observational studies. So, thanks.  
3 DR. MCNEIL: Thank you very much for  
4 those comments.  
5 What I would like to do now is, this  
6 committee is blessed to have a number of  
7 methodologists, a number of practitioners, and a  
8 number of representatives from consumer and other  
9 groups here, so I would like us to talk to each  
10 other. I would also encourage those of you who  
11 are in the audience not to leave on the off chance  
12 that we have another question to ask you, but at  
13 this point we will be talking mostly with each  
14 other, and while we may throw out a question, I  
15 expect a lot of the dialogue to be among ourselves  
16 at this point. Jerry.  
17 DR. JARVIK: I just have a quick  
18 question as to how best answer these questions.  
19 What parameters should we use to decide whether  
20 something is either poor or very good on these  
21 scales? Should we use, as you suggested, the  
22 Cochrane collaboration criteria or something else?  
23 DR. PHURROUGH: Let me take a try at  
24 that. In all our decisions where we are grading  
25 evidence, we usually have a difficult time in our

00220

1 organization clearly defining exactly the  
2 standards that we use for assessing whether  
3 evidence is or isn't of good quality, and so we  
4 typically define that within each of our decisions  
5 based upon the particular type of process it is,  
6 the ability to gather information of the process  
7 and so forth.  
8 We have some limitations in saying we  
9 will accept this, this and this standard, or we  
10 will accept American Academy of Dental Physicians  
11 standards, or we will accept NAOA standards, or  
12 any of those numerous organizations who establish  
13 standards, since our selection of one over the  
14 other would seem to be challenged with our being a  
15 government agency, selecting one over the other,  
16 so we have a difficult time doing that.  
17 So this committee in general uses their  
18 own independent determinations of what they  
19 believe to be good and not good evidence, which in  
20 some cases does result in various members of the  
21 committee having different views of what is and  
22 isn't good evidence, and that's about as close as  
23 I can get to you. So you get the, you have the  
24 opportunity to decide for yourself what you  
25 believe to be good and not good evidence.

00221

1 DR. RESNICK: Just on this subject, all  
2 the evidence that's been presented would be Class  
3 III or higher, it's all case series evidence, but  
4 I'm pretty convinced from the evidence that's been  
5 presented that short-term morbidity with these  
6 treatments, that these treatments help short-term  
7 morbidity resulting from compression fractures.  
8 So I'm fairly convinced based on poor quality  
9 evidence, so what number should I put there?  
10 DR. MCNEIL: That's question three.  
11 There are two separate questions when you look at  
12 them, one is how good are the data, that's  
13 question two, and question three is how good are  
14 the outcomes. So it sounds as if you say the  
15 outcomes are pretty good short-term but the data  
16 aren't, it would be high for three and low for  
17 two. Yes?  
18 MR. QUEENAN: I just wanted to make  
19 sure that I had the right understanding of what we  
20 meant when we were saying conservative care, and  
21 it wasn't clear to me whether that was applied  
22 equally or meant the same things as all the  
23 studies we heard about. Sometimes I heard the  
24 word nonoperative care, or some other terminology  
25 was used, so I just wanted to know whether this

00222

1 committee had a common understanding of that term,  
2 since that's the baseline of things that we're  
3 considering.  
4 DR. MCNEIL: Well, I think -- I'll  
5 start that, but I would like perhaps Jerry or Jim  
6 to add to this. We would have to read each one of  
7 the articles and look to see specifically what the  
8 authors meant by conservative care, but my sense  
9 from reading it was that it wasn't exactly the  
10 same in each study, but that it generally meant  
11 nonsurgery.  
12 DR. BURKE: That's exactly right.  
13 DR. MCNEIL: So whatever nonsurgery  
14 means, that is conservative. Any other comments?  
15 MR. QUEENAN: So just to clarify, it  
16 did not include, I assume, other interventions  
17 that might for example be treating the  
18 osteoporosis along with pain?  
19 DR. BURKE: It could have.  
20 DR. ONDRA: I think perhaps a less  
21 confusing term would be nonsurgical care, because  
22 there are times that nonsurgical care is not  
23 conservative.  
24 DR. WEINSTEIN: I've seen the  
25 nonoperative care that was given in the three

00223

1 studies that people talked about, and I was  
2 wondering, what was the nonoperative care in those  
3 studies?  
4 DR. MCNEIL: Do you have that,  
5 Jonathan?  
6 DR. WEINER: It will take me a while.  
7 DR. MARK: Barbara, I'll look too.  
8 DR. MCNEIL: Okay.  
9 DR. KRIST: In Diamond they talked  
10 about like giving Fosamax, calcium, and it was  
11 unclear whether they got physical therapy, and I  
12 don't see if they received that, but they talk  
13 about calcium, Fosamax, which is what I saw as the  
14 key interventions in there, and narcotics. I have  
15 it right here if you want to refer to it again.  
16 MR. QUEENAN: Actually, maybe the  
17 question I should be asking, I can understand that  
18 it would probably vary from study to study. Since  
19 I am not a doctor or physician, I'm interested in  
20 knowing whether the experts here think that it  
21 matters to the interpretation.  
22 DR. BURKE: Yes, it does matter.  
23 DR. KRIST: I have it here, if you want  
24 me to read it. Calcium and (inaudible).  
25 DR. MCNEIL: That's the Diamond study.

00224

1 DR. MCNEIL: Did you want to say  
2 something, Dr. Burke, just to be explicit?  
3 DR. BURKE: No. Just because if you're  
4 comparing something to something else, if you  
5 don't have, for example, systematic pain  
6 management done by pain professionals, you will  
7 get a very different quality of results in your  
8 comparison results, or if you don't do pain  
9 management at all, or if you let the surgeons do  
10 pain management, and most of these studies have no  
11 comparison at all, so it's moot.  
12 DR. MARK: David Mark from Blue Cross.  
13 Just briefly, the Kasperk study says that both  
14 groups, both the observational and the surgical  
15 group received medical treatment daily, standard  
16 dose of bisphosphonate, calcium, vitamin B, and a  
17 recommendation for supervised physiotherapy once a  
18 week, but no other evidence about compliance,  
19 adherence, stuff like that.  
20 DR. MCNEIL: Thank you.  
21 DR. WEINSTEIN: One of the things I'm  
22 having a hard time with, I think Josh may have  
23 taken my comments and thrown them away about  
24 radiologists, but the issue is that this is a  
25 problem confounded by different disciplines caring



00225

1 for different parts of the disease. It is a  
2 metabolic disease and hormone replacement therapy  
3 or calcium therapy, monitoring those things in a  
4 clinical practice, versus an intervention that's  
5 technically done by an orthopedist, neurosurgeon  
6 or a radiologist, and I think the issue of the  
7 comorbidities that are often associated with older  
8 people, none of these results are adjusted for  
9 baseline differences, none of these results are  
10 adjusted to my knowledge for comorbidities.  
11 There's just so much confounding here because of  
12 the management of these difficult patients, and I  
13 think that's part of the problem.  
14 I don't think they are able to do these  
15 studies well because these patients are in  
16 different places and different kinds of practices  
17 that don't seem to me, this is the first time I've  
18 heard of a radiologist running a clinical  
19 practice, I didn't know that was occurring so I  
20 apologize, but I think that's an unusual  
21 occurrence in many places. So if you manage  
22 osteoporosis, you manage their fractures and if  
23 something happened, I suppose you would do their  
24 surgery, I don't know.  
25 The issue is that these are complicated

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1 patients that require co-intervention by lots of  
2 disciplines. I think Dr. Garfin tried it once  
3 with the metabolic people, with the idea that that  
4 may be where the people should be enrolled from,  
5 and I think that's actually probably right.  
6 Primary care doctors and endocrinologists are  
7 probably the people who should be enrolling these  
8 patients in trials for the interventionalists.  
9 I feel like I am a clinical trial  
10 (inaudible) funded by NIH for spine problems and  
11 it is not easy, but it clearly is doable. And the  
12 reason it is, it doesn't work is because of us,  
13 the clinicians, and not having that echo poise  
14 that Dr. Talmadge talked about. But I also think  
15 in this particular population, because of the  
16 comorbidity and multiple disciplines that are  
17 needed to care for these patients, it creates a  
18 lot of difficulty in actually setting this up, and  
19 I would argue that the failure was in thinking  
20 this out ahead of time and how to actually follow  
21 that process for the benefit of the patient, not  
22 for the benefit of treating one fracture or three  
23 fractures, but treating that patient. I think  
24 that's where these data just get lost on me, and  
25 the fact that I can't come away with more than

00227

1 level one data.  
2 But that compassionate need to take  
3 care of the patient in pain, obviously as a  
4 physician, we all feel that compassionate need,  
5 but does compassionate need drive science or does  
6 science drive compassionate need, and what often  
7 happens is compassionate need drives treatment,  
8 and science then comes back like the bypass or  
9 something that Josh was mentioning in oral  
10 surgery, where there is a tremendous compassion  
11 for doing the procedure, the randomized trial  
12 doesn't work. It didn't mean there weren't a lot  
13 of editorials in the New England Journal about it  
14 filled with compassion, but that procedure is no  
15 longer being done for the most part.  
16 DR. WEINER: To build on  
17 Dr. Weinstein's statement, a comment as a  
18 professor of public health. Usually on these  
19 boards I make a comment that I don't really care  
20 about the neurosurgeon, orthopedist or  
21 interventional neuroradiologist, it's about the  
22 patient, it's about the population.  
23 And I would urge the committee to read  
24 the letter from Dr. Sam Ho, the medical director  
25 for, to the best of my knowledge, the largest or

00228

1 second largest Medicare HMO organization, a very  
2 thoughtful letter that says hey, it seems to work,  
3 but that's not enough. And I think as we move  
4 toward, we ain't seen nothing yet, you know,  
5 before the baby boomers come on board, as we move  
6 toward limited resources, that we need to get this  
7 right and people need that meeting at the high end  
8 retreat you talked about, and it needs to be  
9 across specialties and also with outcomes  
10 researchers and CMS at the table. It needs to be  
11 population-based and I would encourage you to look  
12 at that. Dr. Ho says yes, it seems to work, but  
13 that's not good enough.  
14 I also want to ask the questions but  
15 not right now, it's really more of a statement,  
16 but when does it work, for whom, what are the  
17 indications? There are lots of questions, you  
18 know, once, twice, three times, we can't pay for  
19 it all. And then in the end result, does it  
20 really improve the life, and can we pay for it.  
21 And Dr. Ho's bottom line, by the way, is we need  
22 to start collecting data because it's not good  
23 enough just because it seems to work.  
24 DR. R.G. FESSLER: I think that if in  
25 fact we want to get it right, we're ignoring a

00229

1 significant question that we would have to answer  
2 at the same time, and that is the patients we're  
3 talking about treating are the patients that  
4 failed nonsurgical therapy, I'm not going to call  
5 it conservative because that's an oxymoron. When  
6 you get acute epidural hematoma, conservative  
7 therapy is surgery and aggressive therapy would be  
8 ignoring it and letting the patient die. In this  
9 case our alternative to treating those patients  
10 who failed nonsurgical therapy is an open  
11 thoracotomy, an open laparotomy with multiple  
12 level instrumentation posteriorly. If we want to  
13 get it right, we've got to randomize those  
14 patients too when we do the study.

15 DR. KALLMES: I wanted to address the  
16 question about who's doing it and when, and just  
17 that, I have some insight because I wasn't there  
18 at the beginning with Dr. Jensen. She had that  
19 seminal paper in 1967 which has been cited 276  
20 times in the literature. About three years ago I  
21 read the paper and I made a list of ten things  
22 that were outright, well, I called them lies, they  
23 were wrong in my opinion, how much cement to use,  
24 how many needles do you put in, who do you treat,  
25 does the physical pain matter. All these things

00230

1 have changed in our practice and elsewhere, so  
2 it's a very dynamic practice. How do you select  
3 the patients? We don't even know.  
4 So there is, you know, we have all  
5 these papers where the mean pain goes from 9.5 to  
6 2. I have been in the exam rooms with those  
7 patients. They're 80 years old and they say, you  
8 ask if they have pain and they say I can't really  
9 tell you. Is it a ten, yeah, it's a ten. So I  
10 think there is a lot of bias in how we collect  
11 these data. When they come back, they say how are  
12 you feeling, what's the best your pain has been?  
13 I'm a practitioner, I believe in the procedure, I  
14 really do, but I'm on the inside and I know what  
15 the data are, and they're probably not as good as  
16 people are standing up there saying they are.  
17 DR. PHURROUGH: Being just a country  
18 doc having practiced in Texas and the rest of the  
19 United States, I'm not real clear on what  
20 individual criteria are for deciding a patient is  
21 ready to get the kyphoplasty or vertebroplasty.  
22 Dr. Fessler, you just mentioned patients who have  
23 failed conservative care, and yet we have talked a  
24 lot about this is also an acute procedure and can  
25 relieve acute pain, and then we talk about

00231

1 patients who are two weeks or four weeks or six  
2 weeks, or is it all of these patients? If it's  
3 indicated as a procedure after failed conservative  
4 care, which we've heard some people mention, and  
5 there is a different data set we would need to  
6 evaluate that, and if it's indicated as an acute  
7 procedure, how do you decide whether all patients  
8 who show up immediately with a compression  
9 fracture are acute, are they all indicated for one  
10 of these procedures, or what is indicated? I'm  
11 confused, so someone help out this country doc  
12 here.

13 DR. KALLMES: Dr. Jensen deserves the  
14 credit for attempting to develop this in North  
15 America, and back then we admitted the patients  
16 overnight, you know, all our patients came from  
17 neurosurgeons, patients had to have failed six  
18 weeks of medical therapy, they had to be on  
19 narcotics. And now it's similar to diagnostic  
20 vertebroplasty. That is to say, we don't know  
21 where your pain's coming from but let's give it a  
22 try, so things have really slipped. If you're  
23 doing 500 vertebroplasties a year, you know, what  
24 is your selection criteria? It's highly  
25 different. People say the physical exam is very

00232

1 important. Dr. Jensen and I published, saying you  
2 have to have localized pain to the spinous process  
3 when you came through the door to be a candidate,  
4 and you know, we had no good physiologic mechanism  
5 for that. We hired a nurse practitioner after a  
6 couple years and every single patient that came to  
7 our door had pain on palpation. I watched her  
8 palpating these patients and it was excruciating  
9 to watch.  
10 So, we don't really know how to select  
11 patients. The fact of the matter is if you have  
12 an MRI that has edema, you're in. That's the  
13 great thing about doing vertebroplasty, you've got  
14 to be a card-carrying fracture patient. There is  
15 none of this, well, you really have to have an  
16 MRI, and it's basically, I would say that 99  
17 percent of patients had an MRI and if there's  
18 edema on the MRI, they get the kyphoplasty or  
19 vertebroplasty, that's the fact of the matter. I  
20 think it's also subjective back pain and so forth.  
21 But I think duration of pain, Dr. Diamond studied  
22 (inaudible) patients, and a lot of people do  
23 patients out of the ER now. Is that the right  
24 thing for a patient? I don't know. How long  
25 should we wait? I don't know.



00233

1 DR. MCNEIL: Dr. Jarvik.  
2 DR. JARVIK: I think that he misses an  
3 incredibly important question as to patient  
4 selection. Everybody who was up today or most  
5 everybody said that selecting the right patient to  
6 do the procedure on is important. The problem is,  
7 I don't think we have the data to say who are the  
8 right patients. The best particular is probably  
9 who's going to get better with vertebroplasty,  
10 they're probably the same as who's going to get  
11 better without vertebroplasty, you know, duration,  
12 is likely important, age, I mean, there are lots  
13 of covariants which are worth looking at. But I  
14 am not convinced and the problem is we don't have  
15 a series with a control group to say, well, yes,  
16 there clearly is a difference between those  
17 treatment options.  
18 DR. MCNEIL: Could I ask, which way  
19 does the age go that you're referring to?  
20 DR. KALLMES: I was very surprised to  
21 see that one of the Kyphon studies, Kasperk I  
22 think, greater than one year pain for all those  
23 patients. That's not practice in the U.S. I  
24 mean, one fraction of our patients have had pain  
25 for more than a year, so we don't treat chronic

00234

1 fractures. I think that, you know, six weeks is  
2 probably, six to 12, that's where we get the  
3 patients.

4 DR. PHURROUGH: Does mobility have any  
5 bearing? A couple people mentioned, and I think  
6 it was the Kasperk study that said you have to  
7 have this immobile sitting, supine --

8 DR. KALLMES: To my knowledge, it has  
9 no role in vertebroplasty practice, it may be in  
10 kyphoplasty practice, but having dynamic fracture  
11 is just the cure-all, and I --

12 DR. PHURROUGH: Do all these produce  
13 disparate results if they don't have these  
14 particular findings?

15 DR. KALLMES: No. People have  
16 published that cavities do better and, you know,  
17 (inaudible) necrosis, and that's very  
18 underdiagnosed. If you look at a plain film, it's  
19 great to have a cavity, but when you put cement in  
20 you frequently see cavity, but nobody has studied  
21 that, and it's usually felt to be a good  
22 prognostic indicator, patients tend to do better  
23 with cavity, although in our data patients get  
24 more subsequent fractures if they have a cavity.

25 DR. MCNEIL: Dr. Resnick.

00235

1 DR. RESNICK: I have a comment  
2 regarding what Dr. Kallmes just said regarding the  
3 Diamond study. We have been discussing how the  
4 Diamond control population did better than any  
5 other control population, including the patient  
6 population cited or reported by Hall, the medical  
7 cohort patient population, and is probably because  
8 they were acute patients and people are going to  
9 get better in the first couple of days, first  
10 couple of weeks after a fracture. So I think that  
11 in terms of the (inaudible), it seems that the  
12 majority of the studies that show benefit, at  
13 least the comparisons are looking in the subacute  
14 to chronic in the U.S. population.  
15 The other comment I wanted to make is  
16 that while it is true that we don't have high  
17 quality evidence, it also is true that we probably  
18 don't want to throw out the baby with the bath  
19 water in terms of this procedure. A large,  
20 15,000-some-odd patients with kyphoplasty and I  
21 don't know how many thousands of patients with  
22 vertebroplasty have at least documented very good  
23 changes in the SF-36, Oswestry, and visual analog  
24 pain scales, and those changes have been  
25 persistent. Now we can't claim that eventually

00236

1 patients in controls may or may not have gone  
2 there, but based upon the Diamond and Hall study  
3 and the small comparative series from Germany, it  
4 seems that the controls are durable and yes, it's  
5 not high quality evidence, but the absence of  
6 proof is not the proof of absence.  
7 DR. MCNEIL: Dr. Weinstein and then  
8 Dr. Burke.  
9 DR. WEINSTEIN: I was thinking that  
10 patients with these painful compression fractures,  
11 it's very hard for them to do flexion and  
12 extension x-rays, I probably wouldn't put them  
13 through that at 70 or 80 years old.  
14 I think the other issue is how is this  
15 data collected on these people, who's actually  
16 collecting the data in these practices. Having  
17 collected thousands and thousands of data points,  
18 this system is just paper and pencil. What do  
19 they do with missing values? None of the papers  
20 talk about data issues, crossover issues,  
21 failures, things that happen in every study, it  
22 happens in everyday practice. I mean, we can't  
23 have all good results. And so the point is, I've  
24 seen patients in my own practice who've benefitted  
25 from this technology, but is that an excuse not to

00237

1 do a good study? And so, I'm struggling with yes,  
2 we don't want to throw the baby out with the bath  
3 water and not help out our patients, but that's  
4 not in the absence of doing good science.  
5 DR. MCNEIL: Dr. Burke.  
6 DR. BURKE: There is a good reason why  
7 we go to blinded study designs. I mean, you know,  
8 when we did the psychology experiments, the  
9 investigators who were interested in a good result  
10 get good results, okay? That's well known.  
11 That's why we blind, that's why we double blind  
12 studies, for exactly that reason. None of these  
13 studies as far as I know are double blinded,  
14 because you couldn't double blind them. So the  
15 investigators are interested in a particular  
16 result. We know, and studies have been done, that  
17 you can get good results if you don't randomize  
18 and blind your patients. Secondly, who's going to  
19 benefit from the treatments? I brought it up  
20 earlier, the only way to know is to have a set of  
21 necessary and sufficient entry criteria in  
22 patients in the study, that's the only way you're  
23 going to find out who is going to benefit, you  
24 can't just take all comers.  
25 DR. MCNEIL: Did you want to add to

00238

1 that, Dr. Resnick?

2 DR. RESNICK: No.

3 DR. MCNEIL: Jerry.

4 DR. JARVIK: A somewhat separate

5 question, which is, we've heard that one of the  
6 strongest predictors of having another fracture is  
7 having a first fracture, and we see in these  
8 various case series and cohort studies persistent  
9 good functional status and lack of pain

10 development down the road, and I'm just wondering,  
11 why aren't we seeing sort of recurrent pain, you  
12 know, you know, in people on follow-up. A fair  
13 percentage must be developing pain, or doesn't  
14 that happen separately?

15 DR. KALLMES: I was going to talk about  
16 subsequent fractures. At Mayo, 40 percent of our  
17 patients are reduced, they have already had  
18 vertebroplasty. On the one hand you can say  
19 that's great, that means they love us, we really  
20 do a good job. I'm just, I was ignorant about  
21 Dr. Lieberman's study with these surveillance  
22 radiographs so we can catch all the fractures or  
23 not, but we know that we're undercatching all our  
24 fractures and still have a very high bounce-back  
25 rate.

00239

1 DR. FENDRICK: You don't mean reduce,  
2 you mean a second fracture?

3 DR. KALLMES: Yes. I have the only  
4 paper of the six -- I'm sorry, retreatment at the  
5 same level, that's extraordinarily rare, but  
6 patients get fractures at other levels.

7 DR. MCNEIL: 40 percent?

8 DR. KALLMES: Yeah. Actually in our  
9 trial I know this because that was the exclusion  
10 criteria in 40 percent of the patients, they had  
11 already had vertebroplasty and they come back with  
12 recurrent pain from their new fracture.

13 DR. MCNEIL: I just want to make sure I  
14 understand. So 40 percent of your patients come  
15 back?

16 DR. KALLMES: No, that's not what I'm  
17 saying. Of patients that we see, we've already  
18 treated about 40 percent of them, but we've  
19 treated 500 patients over five years, so we see  
20 patients as far back as five years. So I don't  
21 mean to say that there is a 40 percent refracture  
22 rate, I don't know what our refracture rate is  
23 because we don't do surveillance radiographs. We  
24 only get the painful ones that come back, and  
25 there are numbers all over the map in the

00240

1 literature, from as low as 8 percent to 67  
2 percent, I don't know what the number is.  
3 DR. MCNEIL: Would 8 to 10 percent seem  
4 low to you?  
5 DR. KALLMES: I don't know, I have not  
6 systematically looked into that. I would be  
7 surprised if it were as low as that because I  
8 think it depends on how well they're treated with  
9 medical therapy. Are they all getting  
10 teriparatide, probably not, but if they are, then  
11 I would say 80 percent is high, and if they  
12 aren't, I would say it's pretty low.  
13 DR. FENDRICK: One of the things that's  
14 positive to the observational trial is, I think I  
15 would disagree with Dr. Jarvik a little bit, but  
16 one of the good things that you could use in  
17 observational studies is actually predict the  
18 likelihood of a positive effect of that  
19 intervention. Now that doesn't say that it  
20 wouldn't also happen in the control group, but you  
21 don't need a control group in Dr. Lieberman's  
22 study since he has such a richness of data that I  
23 imagine that you have too, Dr. Kallmes, that you  
24 could actually say that the people who may be in  
25 danger, if you have the variables and there are



00241

1 various standards, maybe there is something,  
2 certain variables, and when people are treated at  
3 time zero, that would predict that all of them do  
4 well or none of them do well. So that's something  
5 that you could really do a couple of studies as  
6 you move forward, to find something about, I don't  
7 know, the mechanics or height or age that would  
8 preclude some people right off the bat.

9 DR. SULLIVAN: I've never done this  
10 before, which is disagree with Mark in a public  
11 forum, which I'm pleased to do actually.

12 DR. MCNEIL: Feel free.

13 DR. SULLIVAN: The only thing, I would  
14 say I think he is mostly right, but you have to be  
15 able to have better follow-up to be able to do  
16 what he's suggesting, and with the follow-up that  
17 I'm seeing in these series that are extremely  
18 poor, you can't do what Mark is suggesting. In  
19 theory you can if there is better follow-up data.

20 DR. BURKE: Well, it's not even that,  
21 because you have to control for covariates and  
22 more confounding factors, and in order to do that,  
23 you have to have a lot of sample size to see the  
24 effect.

25 DR. RESNICK: Just getting back to

00242

1 methodological concerns, Dr. Burke mentioned that  
2 the only way to answer the question would be to  
3 have a priori entrance criteria to randomize the  
4 patients as possible. As we've heard from Dr.  
5 Kallmes, they only had a three percent accrual  
6 rate and out of a hundred patients they screened,  
7 only three patients signed on. When we were doing  
8 our fusion guidelines, we saw that in the  
9 methodology that of 1,500 eligible patients, 30  
10 were selected to do the study, and you would  
11 immediately knock that down to a case series type  
12 level of evidence.

13 DR. BURKE: That's correct, but on the  
14 other hand it talks to the generality of your  
15 study rather than the comparison itself, because  
16 you randomize you can still make comparisons, but  
17 how generalizable the treatment would be is  
18 limited by the two patients which you enroll.

19 DR. KALLMES: I would like to respond  
20 to that, that's an excellent point. If we ever do  
21 the trial, I think we would have a tremendous  
22 selection bias in patients with less pain, the  
23 pre-procedure pain level would be extremely low  
24 compared to the 9.5 in most studies and I don't  
25 know how to get around that. Our custom is four

00243

1 weeks, it might possible in 48 hours, is that good  
2 enough for the panel? You know, is 48 hours of  
3 natural history okay? You might need to come back  
4 to that level to get patients in excruciating  
5 pain.

6 DR. MCNEIL: I would like to ask a  
7 question of the clinicians and that is, suppose  
8 either of these procedures diffuse widely, even  
9 more widely than exists right now, just pretend.  
10 Apart from cost, what would be your worst fear  
11 about health outcomes?

12 DR. ONDRA: One of the standards that I  
13 think is fairly used, but my concern really is,  
14 what is the morbidity of treatment versus the  
15 morbidity of nontreatment in that first six-week  
16 to 12-month period, where at least the Class III  
17 to V data suggests there is a pain benefit? We're  
18 sort of getting involved in debating the relative  
19 plausibility of RCTs in this population and  
20 perhaps we're a little off track here.

21 DR. MCNEIL: Could I just push you a  
22 little bit on that? There are a whole bunch of  
23 possible side effects that occur in the first  
24 short term. Are some of those, if we start doing  
25 this procedure more and more, have some of those

00244

1 really been overlooked? I forgot what we said,  
2 like emboli of the brain or whatever?  
3 DR. ONDRA: Those are the things that  
4 we talk about, embolism of the brain, narcotic  
5 use, pneumonia rates, pressure ulcerations of the  
6 skin between different populations, the need for  
7 surgical intervention for extrapitiation, there is  
8 a whole host of things that would be very  
9 important, not just how much height restoration,  
10 you know, how much angulation, and I think we're  
11 missing some of the important parameters.  
12 DR. MCNEIL: Is that because we just  
13 don't have enough patients on whom those data have  
14 been reported?  
15 DR. ONDRA: I don't think we have  
16 collected the data.  
17 DR. MCNEIL: There has been some,  
18 there's the FDA review. I was trying to figure  
19 out, again, Jerry, you told me about a brain  
20 embolus, didn't you?  
21 DR. JARVIK: No, it was a septic  
22 emboli, but I actually think there is relatively  
23 good evidence about the safety of these procedures  
24 and you can get that information from case series  
25 about the procedure itself, if you have good

00245

1 follow-up. But down-the-road complications, my  
2 biggest fear actually is probably subsequent  
3 fracture rate, which I'm actually somewhat  
4 surprised at the cohort data from the German study  
5 that suggests lower rates of fracture, and I would  
6 like to see more.  
7 DR. ONDRA: And there is a nonexisting  
8 control group.  
9 DR. MCNEIL: Okay.  
10 DR. FENDRICK: One thing I need to hear  
11 from the interventionalists, I think it was  
12 glossed over because there was probably a  
13 variation of practice in this need for general  
14 anesthesia. These are old folks. I'm not worried  
15 about safety in all the things that were listed on  
16 all the slides in the cohort study, but I heard  
17 one physician only does locals for  
18 vertebroplasties, some people do them for  
19 kyphoplasties, a lot of local, some people use  
20 general anesthesia. I think I really kind of  
21 heard from all the experts saying on pain and  
22 outcomes that they're guessing, because it has  
23 never been compared, that many of the outcomes are  
24 going to be comparable. When I have a choice to  
25 put a 77-year-old person of any type under a local

00246

1 or conscious sedation versus general anesthesia, I  
2 think this is huge, and I don't think that has  
3 been discussed at all in terms of the potential  
4 downside risk of one or the other.

5 DR. KALLMES: We do all ours under  
6 moderate sedation and that has been fine. I would  
7 be interested to know how the radiologists feel  
8 about conscious sedation, I think Josh said. I  
9 don't know, but I'd be interested with conscious  
10 sedation.

11 DR. FENDRICK: There were some slides  
12 in the documents and general anesthesia is rare,  
13 is that your --

14 DR. KALLMES: For vertebroplasty, yeah.

15 DR. FENDRICK: I'll try to speak  
16 English. In practice, not in the experts' hands,  
17 is there a difference in anesthesia choice between  
18 the two procedures and if there is, I think if all  
19 other things are equal, it's important for us to  
20 know, because the risk of anesthesia in an  
21 80-year-old in terms of local versus general.

22 DR. KALLMES: Dr. Lieberman said he did  
23 90 percent of his under general anesthesia, I  
24 think.

25 DR. LIEBERMAN: Yes, but that's just a

00247

1 breakdown. Part of that is practice location,  
2 whether I do it at an outpatient facility versus  
3 an inpatient facility. Part of that is also my  
4 anesthesia colleagues, they're a lot more  
5 comfortable with an 80-year-old face down with a  
6 tube in under general anesthetic than they are  
7 with an 80-year-old face down under neuroleptic;  
8 if something should happen, they can't intubate  
9 that patient, so they insist that we do it more  
10 often under general than under local.  
11 DR. KALLMES: Even for vertebroplasty?  
12 DR. LIEBERMAN: Even for  
13 vertebroplasty, yeah.  
14 DR. KALLMES: That's unusual, though.  
15 DR. LIEBERMAN: Now again, it's  
16 practice location. The anesthesiologist will say  
17 well, if we're doing it in the angio suite or  
18 we're doing it over at Carnegie or Beechwood, I  
19 don't want to drag my anesthetic machine over  
20 there, so it's okay to do it over there under  
21 local anesthesia.  
22 (Laughter, followed by inaudible  
23 colloquy.)  
24 SPEAKER: There has been one death I  
25 know of from myocardial infarction, there's been

00248

1 several cases of paraparesis, the one case series  
2 (inaudible) some of these series, I think Dr. Cadu  
3 mentioned the (inaudible). And then I worry about  
4 the long-term secondary fracture rates, which  
5 we've heard from Dr. Lieberman being 11 percent in  
6 the primary, 45 percent in the secondary  
7 osteoporosis, and Dr. Freiberg, 26 percent, with  
8 53 percent in adjacent segments. As we get an  
9 older-aged population that will live longer, what  
10 will be the implications of that in taking care of  
11 these patients? I don't know, but those are  
12 things that try to answer your question.  
13 DR. KRIST: I was going to say that as  
14 a family physician, I see a different group of  
15 patients than the severity of patients we're  
16 hearing about for this procedure. But more of my  
17 concern, and some speaker already said it, is that  
18 patients who you wouldn't really think about doing  
19 this on will receive it. So most of these  
20 studies, they're saying that people have been on  
21 six weeks, or one or two weeks of medical  
22 management, and failed therapy diffuses a lot  
23 more. And as patients expect this or learn about  
24 it, as physicians know about it, then a whole  
25 group of patients we wouldn't even think about



00249

1 doing this on, will receive it. In my community  
2 we're sending the patient to a radiologist, that's  
3 the group in our community who does it, I just  
4 write a referral for them to go get  
5 vertebroplasty, and they come back and have had it  
6 done. It's not a very systematic process for  
7 figuring out who gets it and who doesn't.  
8 DR. R.G. FESSLER: Jim, I want to  
9 respond to some of your concerns, because I think  
10 they may not accurately represent the implications  
11 of the data. You said there was in 75 percent,  
12 but in fact only one percent or 1.5 percent are  
13 symptomatic. You know, my concern actually is,  
14 and before I go into that is whatever the  
15 percentage is, 10 to 40 percent, whatever the  
16 refracture rate is, that may not be any different  
17 than the natural history of the disease, and that  
18 may be all that we're seeing, the fact of natural  
19 history of osteoporosis in an aging population.  
20 So my concern is that in the hundreds  
21 of patients that I have done and in following them  
22 over the years, it's my distinct impression that  
23 in fact morbidity and mortality is lower in these  
24 patients than it is if you let it follow its  
25 natural history, and I'm afraid of missing that

00250

1 fact by talking about the potential morbidity in  
2 minuscule percentages when we do know that  
3 morbidity of an 80-year-old patient who's  
4 bedridden for six weeks is.  
5 DR. WEINSTEIN: I think Dr. Talmadge  
6 from Kyphon did a nice summary of sort of what's  
7 happening in the osteoporosis literature and  
8 associated with these nontreated patients, I think  
9 she's right, that there is a significant  
10 morbidity. I was trying to answer the question of  
11 what the concerns are and I think the cement  
12 leakage, although many argue it is not a problem,  
13 I don't know. I mean, in most cases it turned out  
14 not to be a problem.  
15 But as we're having this open  
16 discussion, when I looked at the Medicare  
17 guidelines for doing the procedure and the stuff  
18 that was in the material that was mailed to us  
19 from the June 15th, 1999 document about what are  
20 the indications, what are the procedures under  
21 Medicare's rules and how this should be done, it  
22 talks about, and I quote, "The decision for  
23 treatment should be multidisciplinary and take  
24 into consideration the local and general extent of  
25 the disease." And I sort of thought about that as

00251

1 what I was getting to before; health care today is  
2 not about just a discipline taking care of a  
3 patient, but that's sort of the way we practiced  
4 for a long time, and I think this is an example  
5 that osteoporosis is a disease that is more than  
6 just an interventional type of problem, but  
7 clearly the new medications are going to have a  
8 role as was just pointed out, and the evaluation  
9 of osteoporosis with MRI, and what I worry about  
10 is we talk about these things in isolation of the  
11 patient as a whole, which wasn't the intent of the  
12 coverage here.

13 And I don't know how that would help  
14 this, but my understanding is that we would have  
15 thought about a multidisciplinary approach to this  
16 problem and not sort of sending it to the guy who  
17 does this, or helps with the pain, and if we do a  
18 lot of medicine, maybe we would have had the  
19 ability to treat and follow these patients a  
20 little bit differently. I think the physicians  
21 who are responding today and are talking about  
22 their results all have altruistic goals and have  
23 no malfeasance of trying to do something wrong,  
24 they are trying to help patients.  
25 But the system, we cannot pay for

00252

1 things, and I would argue this is under your  
2 guidelines as well, certainly if a long-term  
3 reduction study and other things were done under  
4 protocol and paid for, \$75,000 a case for that one  
5 reduction study, there is no reason we couldn't  
6 continue on getting the kind of data that we need  
7 to help these patients in the right way. I think  
8 this talk is circular and all of us involved in  
9 trials realize how difficult this is, but that's  
10 an excuse to not do it. You have the ability to  
11 set the guideline and the rules to help pay for  
12 things that aren't being done, to collect the data  
13 and come back with an answer, it sounds like  
14 pretty quick given the number of these things that  
15 are being done. So I would argue that given your  
16 directive in '99, we haven't really followed that  
17 and we need to consider doing that with payment,  
18 and get the answers and come back and discuss it.  
19 Otherwise, we're just going to be going round and  
20 round in circles.

21 DR. BURKE: I mean, as a doctor  
22 practicing in the community too, the heterogeneity  
23 of pain management in the community is quite  
24 large. Some docs do a great job in pain  
25 management, some docs do a terrible job in pain

00253

1 management, and that in itself is a tremendous  
2 bias. It seems to me that if you're putting it in  
3 the context of professional anesthesiologists or  
4 whatever, who specialize in pain management and  
5 look at this procedure after they have had the  
6 pain management, and in coordination with  
7 systematic professional pain management, we might  
8 see something better.  
9 DR. MCNEIL: That's a control group.  
10 So, Jerry, tell me what the sample size you needed  
11 for your RCT, what was it?  
12 DR. JARVIK: It was originally powered  
13 at around 280, is that right?  
14 DR. KALLMES: 294. Our primary outcome  
15 was a Rowley scale, a modified Rowley scale, it  
16 was not pain, and it was my belief that the Rowley  
17 changes, but with vertebroplasty we go from about  
18 19 of 23 to 11 of 23, so I think 294 is, and doing  
19 all the control interventions, they might go to 19  
20 and 11 as well, but I think it's probably over,  
21 and 294 was the quickest.  
22 DR. MCNEIL: And what was the end  
23 point?  
24 DR. KALLMES: I'm sorry, we have  
25 another dirty little secret, one-month crossover,

00254

1 you could cross over after a month.  
2 DR. JARVIK: And we were following out  
3 for a year.  
4 DR. MCNEIL: Okay. Sean.  
5 Dr. SULLIVAN: Just to comment on the  
6 sample size, remember the reduction series study  
7 that was powered to 2,500 patients initially which  
8 had a 25 percent crossover, and they experienced a  
9 five percent crossover, and so they were able to  
10 (inaudible).  
11 DR. KALLMES: Let me say that the  
12 impediments to doing prospective research on  
13 vertebroplasty is much less today than it has been  
14 in the past, at least from a regulatory  
15 standpoint, because until cement was approved for  
16 vertebroplasty, and Kyphon affiliates were the  
17 first ones to get it, but that made my life so  
18 much easier because I didn't have to wait  
19 (inaudible) and now you have much more leeway on  
20 what kind of study design you can do, a lot of  
21 people have mentioned difficulty with the IRB, so  
22 you can be more creative with study design.  
23 DR. MCNEIL: Other issues? Comments?  
24 Well, if that's the case, then we should perhaps  
25 go to the questions. So what I'm going to do is,

00255

1 you all have cards.  
2 DR. KALLMES: We are nonvoting members,  
3 but we vote?  
4 DR. PHURROUGH: Everyone does, and we  
5 will determine how to count.  
6 DR. MCNEIL: Okay. Assuming everybody  
7 has one, two, three, four and five, and if you  
8 don't, please say so. I will read the questions,  
9 first for vertebroplasty and then for kyphoplasty,  
10 and then everybody will just raise the number that  
11 they think reflect their opinion, and keep it held  
12 because we have to have basically two people count  
13 it, right?  
14 So the first question is on  
15 vertebroplasty. How well does the evidence  
16 address the effectiveness of vertebroplasty for  
17 patients with compression fracture as compared  
18 with conservative care, realizing that there is  
19 some ambiguity in what conservative care is, going  
20 from one, poorly, to five, very well? Just hold  
21 up your scores.  
22 (All six voting members voted two; of  
23 nonvoting members, four voted two, one voted  
24 three, and two voted four.)  
25 DR. MCNEIL: And I'm not voting.

00256

1 DR. PHURROUGH: I notice some of you  
2 straining to write these numbers down. We will  
3 produce those and they will be available for you  
4 as soon as the meeting is over. You can still  
5 strain if you want, but you can also relax.  
6 DR. MCNEIL: Now this question relates  
7 to data, not outcomes. How confident are you in  
8 the validity of the scientific data on the  
9 following outcomes with respect to vertebroplasty  
10 for patients with, and I'm first going to ask  
11 about acute and subacute compression fractures, so  
12 asking about the data, short-term morbidity,  
13 again, one to five?  
14 DR. RESNICK: In terms of this  
15 question, are we referring to the short-term  
16 morbidity of the procedure or the short-term  
17 morbidity of the fracture? Is this an efficacy or  
18 is this a safety question?  
19 DR. MCNEIL: This is an efficacy  
20 question, is it not?  
21 DR. WEINER: And from here on you're  
22 going to ask us twice, once for acute/subacute and  
23 then a second time for chronic?  
24 DR. MCNEIL: Yes, acute and then  
25 chronic, would that be easiest? Do you want to go



00257

1 down or across?  
2 DR. BURKE: Either way is fine.  
3 DR. MCNEIL: I will go down. So, how  
4 valid are the scientific data with respect to  
5 short-term morbidity for acute and subacute  
6 fractures?  
7 (Of the voting members, one voted one  
8 and five voted two; of nonvoting members, one  
9 voted one, one voted two, three voted three, and  
10 two voted four.)  
11 DR. MCNEIL: How about long-term  
12 morbidity? Long-term morbidity is two or more  
13 years.  
14 (Of the voting members, one voted one  
15 and five voted two; of nonvoting members, one  
16 voted one, three voted two, and three voted  
17 three.)  
18 DR. MCNEIL: How about mortality?  
19 DR. SULLIVAN: Is that 30-day  
20 mortality?  
21 (Inaudible colloquy.)  
22 DR. MCNEIL: Hold on.  
23 DR. PHURROUGH: This particular  
24 question is asking the validity of the data in  
25 measuring these particular outcomes in patients

00258

1 who have undergone vertebroplasty, so it is the  
2 effect of vertebroplasty on mortality.  
3 DR. MCNEIL: Remember, this question  
4 number two is about the data and our belief in the  
5 goodness of the data. Question three is about the  
6 effect on these various outcomes, so how good are  
7 the data is question two. So how good do the data  
8 describe the effectiveness of this procedure on  
9 mortality?  
10 DR. R.G. FESSLER: But that doesn't  
11 answer the question.  
12 DR. PHURROUGH: It could have no effect  
13 at all, it could have a terrible effect or marked  
14 increase in mortality, and if there's no data,  
15 then you would vote one on that question, if the  
16 data that has been reviewed has no information on  
17 mortality at all, then your vote is one. If there  
18 is no data on mortality for vertebroplasty, then  
19 your vote is one. If there is some data, you are  
20 not comfortable with the data, then something  
21 higher than one. If there is really good data on  
22 the effect on mortality, then your answer would be  
23 five.  
24 The next question will say how does  
25 vertebroplasty affect mortality, the outcome of

00259

1 mortality, and if you say there is no effect, then  
2 your answer is five. So this question is, is  
3 there data, and the next question is, what's the  
4 effect on the outcomes. So we're just talking  
5 about is there data.  
6 DR. KALLMES: On acute and subacute.  
7 DR. MCNEIL: Correct.  
8 (Of the voting members, three voted one  
9 and three voted two; of nonvoting members, one  
10 voted one, four voted two, and two voted three.)  
11 DR. MCNEIL: Were there any data on  
12 mortality, just as an aside?  
13 DR. PHURROUGH: You can't challenge the  
14 vote.  
15 DR. MCNEIL: I can't challenge the  
16 vote, I'm sorry. All right. So, this question  
17 relates to the data on mobile and functional  
18 status, again, acute and subacute.  
19 (All voting members voted two; of  
20 nonvoting members, three voted two, three voted  
21 three, and one voted four.)  
22 DR. MCNEIL: Now pain, pain relief.  
23 (Of the voting members, five voted two,  
24 and one voted three; of nonvoting members, one two  
25 voted two, two voted three, and three voted four.)

00260

1 DR. MCNEIL: Now we're going to do the  
2 very same questions with regard to chronic  
3 compression fracture. So, the data on short-term  
4 morbidity. And remember, chronic, according to  
5 this particular set of definitions is defined on  
6 the back as greater than six months.  
7 (All voting members voted two; of  
8 nonvoting members, four voted two, three voted  
9 four.)  
10 DR. MCNEIL: How about long-term  
11 morbidity?  
12 (Of the voting members, one voted one  
13 and five voted two; of nonvoting members, one  
14 voted one, five voted two, and one voted three.)  
15 DR. MCNEIL: Mortality?  
16 (Of the voting members, three voted one  
17 and three voted two; of nonvoting members, two  
18 voted one, three voted two, and two voted three.)  
19 DR. MCNEIL: Mobility and functional  
20 status.  
21 (All voting members voted two; of  
22 nonvoting members, six voted two and one voted  
23 three.)  
24 DR. MCNEIL: Pain relief.  
25 (Of the voting members, five voted two

00261

1 and one voted three; of nonvoting members, four  
2 voted two, two voted three, and one voted four.)  
3 DR. MCNEIL: Now we're going to move to  
4 question three, which goes from the data to the  
5 actual effect on outcomes. That question reads,  
6 how likely is it that vertebroplasty will  
7 positively affect the following outcomes?  
8 DR. RESNICK: And positive effects is  
9 high?  
10 DR. MCNEIL: Very likely is five, yes.  
11 DR. JARVIK: If you thought there was  
12 not good evidence, on this scale of not likely to  
13 very likely, if we don't know the evidence, what  
14 are we supposed to say?  
15 DR. BURKE: If there is no good  
16 evidence, then the likelihood of effect --  
17 DR. JARVIK: But there still may be,  
18 you know, good evidence. You may be convinced in  
19 your heart of hearts that it's going to work  
20 without good evidence.  
21 DR. MCNEIL: Then you would vote five.  
22 DR. BURKE: That's this question here.  
23 DR. MCNEIL: Then you would answer a  
24 five, Jerry, but you would be wrong -- that was a  
25 joke. Okay. So for your acute and subacute

00262

1 compression fractures, short-term morbidity, in  
2 your heart of hearts.  
3 (Of the voting members, two voted  
4 three, three voted four, and one voted five; of  
5 nonvoting members, one voted three, one voted  
6 four, and five voted five.)  
7 DR. MCNEIL: Long-term.  
8 (Of the voting members, one voted two,  
9 three voted three, and two voted five; of  
10 nonvoting members, one voted one, two voted three,  
11 and four voted four.)  
12 DR. MCNEIL: Mortality.  
13 (Of the voting members, two voted one,  
14 one voted two, and three voted three; of nonvoting  
15 members, one voted one, four voted three, and two  
16 voted four.)  
17 DR. MCNEIL: Functional status and  
18 mobility.  
19 (Of the voting members, one voted  
20 three, four voted four, and one voted five; of  
21 nonvoting members, three voted three and four  
22 voted five.)  
23 DR. MCNEIL: Pain relief.  
24 (Of the voting members, one voted  
25 three, two voted four, and three voted five; of

00263

1 nonvoting members, one voted three, two voted  
2 four, and four voted five.)  
3 DR. MCNEIL: Chronic compression  
4 fracture, same thing, short-term morbidity.  
5 (Of the voting members, one voted three  
6 and five voted four; of nonvoting members, five  
7 voted three and two voted four.)  
8 DR. MCNEIL: Long-term.  
9 (Of the voting members, four voted  
10 three and two voted four; of nonvoting members,  
11 one voted one, five voted three, and one voted  
12 four.)  
13 DR. MCNEIL: Mortality.  
14 (Of the voting members, one voted one,  
15 three voted two, and two voted three; of nonvoting  
16 members, one voted one, one voted two, four voted  
17 three, and one voted four.)  
18 DR. MCNEIL: Mobility and functional  
19 status.  
20 (Of the voting members, four voted  
21 three and two voted four; of nonvoting members,  
22 five voted three and two voted four.)  
23 DR. MCNEIL: Pain relief.  
24 (Of the voting members, one voted three  
25 and five voted four; of nonvoting members, two

00264

1 three and five voted four.)  
2 DR. MCNEIL: So, the next one is a net  
3 health benefit, how confident are you that  
4 vertebroplasty will produce a clinically important  
5 net health benefit for patients with compression  
6 fracture compared to conservative care, and we  
7 will first do acute or subacute.  
8 (Of the voting members, one voted two,  
9 three voted tree, and two voted four; of nonvoting  
10 members, one voted two, two voted three, one voted  
11 four, and three voted five.)  
12 DR. MCNEIL: How about chronic?  
13 (Of the voting members, three voted two  
14 and three voted three; of nonvoting members, one  
15 voted two, three voted three, and three voted  
16 four.)  
17 DR. MCNEIL: Moving on, how likely on  
18 the basis of the literature presented is it that  
19 the results of vertebroplasty in the treatment for  
20 relief of pain and improvement of ability to  
21 function for patients with compression fracture  
22 can be generalized to the Medicare population?  
23 (Of the voting members, three voted  
24 two, one voted three, and one voted four; of  
25 nonvoting members, four voted four and three voted



00265

1 five.)  
2 DR. MCNEIL: Okay, how about to  
3 physicians in community practice?  
4 (Of the voting members, three voted  
5 two, one voted three, and two voted four; of  
6 nonvoting members, one voted two, one voted three,  
7 four voted four, and one voted five.)  
8 DR. MCNEIL: So, we've got the tally  
9 and we are not going to allow anybody to vote  
10 twice on this particular subject. We're going to  
11 go on now to kyphoplasty, so it's exactly the same  
12 set of questions, I think, and some of you would  
13 probably like to just use ditto.  
14 DR. BURKE: I move that we use the same  
15 set of results for the second voting.  
16 DR. ONDRA: Second.  
17 DR. MCNEIL: Any discussion? Is there  
18 anybody who disagrees with the motion?  
19 MR. QUEENAN: The motion is for all of  
20 the questions?  
21 DR. BURKE: Same set of questions, same  
22 results.  
23 DR. WEINSTEIN: I was just thinking  
24 about the morbidity, it would change my score on  
25 that question.

00266

1 DR. BURKE: Then let's do it.  
2 DR. MCNEIL: Okay. So, the first one,  
3 how well does the evidence address the  
4 effectiveness of kyphoplasty for patients with  
5 compression fractures as compared with reasonable  
6 care -- conservative care, I'm sorry.  
7 (All six voting members voted two; of  
8 nonvoting members, three voted two, two voted  
9 three, and two voted four.)  
10 DR. MCNEIL: So, how confident are you  
11 of the validity of the scientific data on the  
12 following outcomes, for kyphoplasty, for patients  
13 with acute and subacute fractures? Short-term  
14 morbidity.  
15 (Of the voting members, five voted two  
16 and one voted three; of nonvoting members, four  
17 voted three and three voted four.)  
18 DR. MCNEIL: Long-term.  
19 (All six voting members voted two; of  
20 nonvoting members, one voted one, four voted two,  
21 one voted three, and one voted four.)  
22 DR. MCNEIL: Mortality.  
23 (Of the voting members, three voted one  
24 and three voted two; of nonvoting members, one  
25 voted one, five voted two, and one voted five.)

00267

1 DR. MCNEIL: Mobility and functional  
2 status.  
3 (Of the voting members, five voted two  
4 and one voted three; of nonvoting members, three  
5 voted two, two voted three, and two voted four.)  
6 DR. MCNEIL: Pain relief.  
7 (Of the voting members, five voted two  
8 and one voted three; of nonvoting members, two  
9 voted two, two voted three, and three voted four.)  
10 DR. MCNEIL: So now we'll do chronic  
11 compression fractures, same set of indications,  
12 short-term morbidity.  
13 (Of the voting members, five voted two  
14 and one voted three; of nonvoting members, two  
15 voted two and five voted three.)  
16 DR. MCNEIL: Long-term.  
17 (All six voting members voted two; of  
18 nonvoting members, one voted one, four voted two,  
19 and two voted three.)  
20 DR. MCNEIL: Mortality.  
21 (Of the voting members, three voted one  
22 and three voted two; of nonvoting members, one  
23 voted one, five voted two, and one voted five.)  
24 DR. MCNEIL: Mobility.  
25 (All six voting members voted two; of

00268

1 nonvoting members, four voted two and three voted  
2 three.)  
3 DR. MCNEIL: Pain relief.  
4 (All six voting members voted two; of  
5 nonvoting members, three voted two and four voted  
6 three.)  
7 DR. MCNEIL: Moving to question three,  
8 how likely is it that kyphoplasty will positively  
9 affect the following outcomes when compared to  
10 conservative care for patients with acute and  
11 subacute compression fractures, same set, short-term  
12 morbidity.  
13 (Of the voting members, two voted  
14 three, three voted four, and one voted five; of  
15 nonvoting members, three voted three, two voted  
16 four, and two voted five.)  
17 DR. MCNEIL: Long-term.  
18 (Of the voting members, one voted two,  
19 two voted three, and three voted four; of  
20 nonvoting members, one voted two, four voted  
21 three, and two voted four.)  
22 DR. MCNEIL: Mortality.  
23 (Of the voting members, one voted one,  
24 two voted two, one voted three, and two voted  
25 four; of nonvoting members, one voted one, three

00269

1 voted two, two voted three, and one voted four.)  
2 DR. MCNEIL: Mobility and functional  
3 status.  
4 (Of the voting members, one voted two  
5 and five voted four; of nonvoting members, six  
6 voted three and one voted five.)  
7 DR. MCNEIL: Pain relief.  
8 (Of the voting members, one voted  
9 three, three voted four, and one voted five; of  
10 nonvoting members, one voted three, three voted  
11 four, and three voted five.)  
12 DR. MCNEIL: Okay. We will move to  
13 chronic compression fractures, same thing,  
14 short-term morbidity.  
15 (Of the voting members, two voted three  
16 and four voted four; of nonvoting members, six  
17 voted three and one voted four.)  
18 DR. MCNEIL: Long-term.  
19 (Of the voting members, one voted two,  
20 three voted three, and two voted four; of  
21 nonvoting members, one voted one, five voted  
22 three, and one voted four.)  
23 DR. MCNEIL: Mortality.  
24 (Of the voting members, two voted one,  
25 three voted two, and one voted three; of nonvoting

00270

1 members, one voted one, five voted two, and one  
2 voted four.)  
3 DR. MCNEIL: Mobility and functional  
4 status.  
5 (Of the voting members, three voted  
6 three and three voted four; all seven nonvoting  
7 members voted three.)  
8 DR. MCNEIL: Pain relief.  
9 (Of the voting members, two voted three  
10 and four voted four; of nonvoting members, four  
11 voted three and three voted four.)  
12 DR. MCNEIL: Okay. Now, how confident  
13 are you that kyphoplasty will produce a clinically  
14 important net health benefit for patients with a  
15 compression fracture as compared to conservative  
16 care, acute or subacute compression fracture?  
17 (Of the voting members, one voted two,  
18 three voted three, and two voted four; of  
19 nonvoting members, one voted two, three voted  
20 three, and three voted five.)  
21 DR. MCNEIL: Chronic.  
22 (Of the voting members, two voted two,  
23 three voted three, and one voted four; of  
24 nonvoting members, two voted two, four voted  
25 three, and one voted four.)

00271

1 DR. MCNEIL: Okay. Based on the  
2 literature, how likely is it that the results of  
3 kyphoplasty in the treatment of relief of pain and  
4 improvement in the ability to function in patients  
5 with compression fractures can be generalized to  
6 the Medicare population?  
7 (Of the voting members, three voted  
8 two, one voted three, and two voted four; of  
9 nonvoting members, four voted four and three voted  
10 five.)  
11 DR. MCNEIL: And to physicians in  
12 community practices.  
13 (Of the voting members, two voted two  
14 and four voted three; of nonvoting members, three  
15 voted two, two voted three, one voted four, and one  
16 voted five.)  
17 DR. MCNEIL: We have one more piece of  
18 business before we finish, and that is to start  
19 with the right hand of the table, and we will ask  
20 people for a sentence or two about why they made  
21 the judgments that they made, and if the spirit  
22 moves you, you can say ditto occasionally.  
23 DR. WEINSTEIN: Ditto.  
24 DR. MCNEIL: But not you, you're the  
25 only one who can't.

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1 DR. WEINSTEIN: Thank you for having  
2 us. I think the participants in this panel spoke  
3 to the limitations of the literature. We have  
4 clinical practice and we have the science of  
5 clinical practice, and as we look back on the past  
6 we always like making it better than they  
7 currently are, but that's the state of the art and  
8 I voted the way I did because of the state of the  
9 art as it exists today.

10 DR. JARVIK: I want to primarily echo  
11 that. I voted what I thought was based on the  
12 existing evidence and my hope is that this will be  
13 an opportunity for CMS to improve that evidence by  
14 partnering essentially with clinical trials.

15 DR. KALLMES: Much as I would have  
16 liked to have given more information on the  
17 patients in our study, as a clinician, I have I  
18 think fairly high confidence that the procedure  
19 works.

20 DR. RESNICK: I believe these are  
21 promising and effective procedures that have to be  
22 better documented.

23 DR. R.G. FESSLER: My decisions were  
24 based on two different criteria. First was the  
25 scientific question and that was based on my



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1 evaluation of our literature as it exists. The  
2 second question was what do you think is actually  
3 going to happen to these patients, and I based  
4 that on my own personal experience following all  
5 of my patients with vertebroplasty, with  
6 preoperative evaluation and evaluation at six  
7 weeks, three months, six months, one year and two  
8 years, and those evaluations include visual analog  
9 scores, Oswestry disability, and SF-36, including  
10 their neurologic exam.

11 DR. SULLIVAN: First, I would like to  
12 thank everyone for the invitation to be here, and  
13 also say that I appreciate the rigor of the  
14 process. I have been the chair of a multistate  
15 private health plan P&T committee for ten years,  
16 so this process has been really eye-opening for me  
17 and I think I'm going to take some things back for  
18 the way we do P&T.

19 With respect to my voting, I think I  
20 was influenced most spectacularly by the very poor  
21 follow-up in the data that we saw relative to  
22 assessing effectiveness. With respect to  
23 mortality, I think I probably gave low scores  
24 because I didn't see any data and scored low  
25 because of that. I'm not a clinician, I have no

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1 experience with the procedure or patients or  
2 family members with this procedure, so I was very  
3 focused on the data that I saw.  
4 MR. QUEENAN: I wasn't particularly  
5 impressed by the data and would like to see it  
6 improved. On the other hand, as a patient or  
7 patient representative, I think we need to listen  
8 to the patients, and having heard about them and  
9 from them, I think that really helped me that this  
10 procedure really does work and will work, and I  
11 think that needs to be taken into consideration.  
12 DR. WEINER: I would second that the  
13 patient input and obviously clinicians who really  
14 do the care. On the other hand, if I were to base  
15 it on my scientific knowledge, we have two or  
16 three ED studies of 30 or 40 each in other  
17 countries, so I think that something that affects  
18 tens of thousands of lives and spends millions of  
19 dollars, I hope that CMS will work with the NIH,  
20 and I think it should be more than maybe, I think  
21 it's really incumbent, and it's going to be even  
22 larger when the baby boomers come on board, and  
23 the science has to be done to do the right thing  
24 and see where these cards may fall.  
25 MS. STARMANN-HARRISON: I would concur

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1 that the scientific data is sorely lacking, but I  
2 also think we have to listen to the clinical  
3 experts and we also have to keep in mind that  
4 improvements in patient care have to be at the  
5 forefront of what we do, so with that in mind, my  
6 votes were in that order. We do need improvements  
7 in the scientific data, and I guess I would look  
8 to CMS if there was any assistance that they could  
9 provide, they have the database to do that.  
10 DR. ONDRA: I agree very much with what  
11 Jim said, the second thing, not the ditto. And I  
12 also agree that we do have a mandate in a sense of  
13 what we need and I can only hope that the funding  
14 to effect that mandate is somewhere in existence.  
15 DR. KRIST: I'll echo what others have  
16 said here, it certainly looks promising, some of  
17 these findings and these trends are relatively  
18 consistent, but I think we need a better designed  
19 study, preferably an RCT.  
20 DR. FENDRICK: I'm impressed by the  
21 dedication and passion of the key opinions here,  
22 and we hear you loud and clear that, at least  
23 taking the votes that I could see, that we are  
24 moved by and confident that if you do the right  
25 studies, the outcomes that you think are going to

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1    happen are likely to happen.

2    DR. BURKE:  My votes were based on  
3    science, and it's just not proven.

4    DR. MCNEIL:  Well, any additional  
5    comments?  Okay.  Steve, do you have some final  
6    words?

7    DR. PHURROUGH:  Yeah, and this is the  
8    final comments about where we go from here.  First  
9    of all, I want to thank the panel.  We purposely  
10   choose people who have various opinions so that we  
11   have this type of vigorous debate so that we can  
12   bring the issues to the forefront, and this kind  
13   of debate is the debate that we're looking for,  
14   and I just want to thank the panel for being open  
15   and willing to challenge each other with the  
16   different issues.  I think it also brings to the  
17   forefront sometimes the challenges of bringing the  
18   methodologist and a clinician together to get the  
19   kinds of data that we want.

20   You know, the field of orthopedics has  
21   moved a long way in the last several years in  
22   collection of data, you've always done an  
23   incredible job in collecting data, you've done a  
24   better job of that I think in the last several  
25   years, but I think perhaps what you heard today

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1 where we've introduced a technology and we're now  
2 saying you need to go back to the beginning of  
3 that technology, or we should have at the  
4 beginning of that technology and done the  
5 appropriate studies. And use that for things that  
6 are beginning now, what are the new technologies  
7 that are coming into the field of orthopedics  
8 today, and that we try to do the right studies  
9 today, and not having this panel meeting five and  
10 seven and ten years from now and saying we don't  
11 have the right data. So I challenge you to look  
12 at those kinds of things, whether it's looking at  
13 the development of protein, or whatever it is  
14 that's happening in orthopedics, let's look at  
15 doing, what are the appropriate studies, and let's  
16 do those trials so that we're not rushing out a  
17 technology before we know what its risks and  
18 benefits are.  
19 And finally, we have some information,  
20 we have some recommendations on quality of  
21 evidence and as I mentioned earlier, we have no  
22 open national coverage determination and had no  
23 plans to open a national coverage determination  
24 for this. We will take this information back and  
25 digest it and see what is the next step for us.

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1 We are certainly interested in stimulating in any  
2 manner that we can further collection of data. If  
3 you have some ideas that you would like to bring  
4 to us in a manner we could help with, we are more  
5 than happy to sit and listen. We don't fund the  
6 administrative cost of doing trials, so if you  
7 want administrative money for doing a trial, we  
8 are not the people to come to. If there is a way  
9 that we can work to stimulate those trials through  
10 helping meet clinical costs or through our  
11 reimbursement coverage process, we are certainly  
12 willing to entertain that. We also have some  
13 relationships with our sister agencies at NIH and  
14 AHRQ, so we would be more than happy to entertain  
15 those kinds of questions and see if we can  
16 stimulate that to occur.  
17 I do expect that over the next several  
18 weeks to months, we will produce some type of  
19 guidance document that will discuss what we think  
20 about how evidence ought to be developed in this  
21 particular field of spinal disease, and those are  
22 always put out in draft form and we will look for  
23 your comments on that.  
24 Now to the assembled groups, thank you  
25 for your attendance, thank you all who presented

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1 and spent your time. We think this has been very  
2 helpful, we look forward to these, I enjoy these,  
3 and I thank you for helping us doing what we think  
4 is the people's business here in ensuring they get  
5 the appropriate treatments. I thank you, and have  
6 safe trips home.  
7 (Whereupon, the meeting adjourned at  
8 3:21 p.m.)  
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